Botanical Sciences 101 (1): 1-40. 2023
DOI: 10.17129/botsci.3072

Received: November 24, 2021, Accepted: May 1, 2022
On line first: November 15, 2022

Review / Revisión

Secondary metabolites in *Viguiera* (Compositae, Heliantheae, Helianthinae) and segregated genera. A review of their biological activities with chemotaxonomic observations

Metabolitos secundarios en *Viguiera* (Compositae, Heliantheae, Helianthinae) y géneros segregados. Una revisión de sus actividades biológicas con observaciones quimiotaxonómicas

Amira Arciniegas[1], Ana-L. Pérez-Castorena[1], Alfonso Romo de Vivar[1], Leobardo Gaona-Gaona[1],
Francisco J. Espinosa-García[2], José Luis Villaseñor[3]*, Guillermo Delgado[1]*

[1] Instituto de Química, Universidad Nacional Autónoma de México, Ciudad de México, México.
[2] Instituto de Investigaciones en Ecosistemas y Sustentabilidad, Universidad Nacional Autónoma de México, Morelia, Michoacán, México.
[3] Instituto de Biología, Universidad Nacional Autónoma de México, Ciudad de México, México.
*Authors of correspondence: vrios@ib.unam.mx; delgado@unam.mx

Abstract

Background: The first monograph of the genus *Viguiera* was published in 1918 by Blake, including about 141 species. Schilling & Panero based on studies of molecular sequences of nuclear Internal Transcribed Spacer and External Transcribed Spacer, as well as cpDNA, proposed to reclassify the genus, relocating its species in at least other nine genera.

Question: Is it possible to identify distinctive patterns between the species of the new classification of *Viguiera s. l.* and the results of the chemical studies reported?

Species considered: Sixty-seven species within the wide *Viguiera* circumscription with chemical studies and biological activities reported.

Results: The species of the genus *Viguiera* synthesize terpenoids represented mainly by sesquiterpene lactones and diterpenes, with triterpenes, polyacetylenes, volatile terpenoids and flavonoids also present. The main types of secondary metabolites were present in the studied species, although some compounds were more frequent than others in some clades.

Conclusion: Germacrolides, heliangolides, furanoheliangolides, tetracyclic diterpenes and flavonoids are the main constituents of *Viguiera* and segregated genera. Some interesting chemotaxonomic relationships are noted. Nevertheless, nondistinctive clear patterns were observed between clades and chemical groups. These results are likely a consequence of the diversity of objectives and methodologies of the reported chemical studies on *Viguiera*.

Key words: Asteraceae, chemotaxonomy, systematics.

Resumen

Antecedentes. La primera monografía del género *Viguiera* fue publicada en 1918 por Blake, incluyendo alrededor de 141 especies. Schilling & Panero en sus estudios sobre la Subtribu Helianthinae (Tribu Heliantheae) basados en secuencias moleculares de los Espaciadores nucleares Transcritos Interno y Externos, así como de cpDNA, proponen reclasificar al género reubicando sus especies en al menos otros nueve géneros.

Pregunta: ¿Es posible identificar patrones distintivos entre las especies de la nueva clasificación de Viguiera s. l. y los resultados obtenidos de los estudios químicos reportados?

Especies consideradas: Sesenta y siete especies en la circunscripción amplia de *Viguiera* con estudios químicos y actividades biológicas informados.

Resultados: Las especies del género *Viguiera s.l.* sintetizan terpenoides, representados principalmente por lactonas sesquiterpénicas y diterpenos, aunque también se reportan triterpenos, poliacetilenos, terpenoides volátiles y flavonoides. En todas las especies estudiadas se obtuvieron los principales tipos de metabolitos, siendo algunos más frecuentes que otros en ciertos clados.

Conclusión: Los principales constituyentes del género *Viguiera s l.* son germacrólidas, heliangólidas, furanoheliangólidas, diterpenos tetracíclicos y flavonoides. Se notan algunas relaciones quimiotaxonómicas interesantes. No obstante, no se observaron patrones distintivos claros entre los clados y grupos químicos de los géneros segregados. Estos resultados son probablemente consecuencia de la diversidad de objetivos y metodologías de los estudios químicos reportados.

Palabras clave: Asteraceae, quimiotaxonomía, sistemática.

The tribe Heliantheae constitutes one of the 43 tribes of the Asteraceae (Compositae) family as it is currently circumscribed (Baldwin 2009). It is considered as part of the "Heliantheae Alliance" along with other 12 tribes, although their relationships remain in discussion. Taxonomically this tribe has been divided in seven subtribes, including the Helianthinae, which comprises *Viguiera* and another 19 genera (Table 1). *Viguiera* was established by Kunth (Nov. Gen. Sp., ed. Fol., 4: 176. 1818) describing one species (*Viguiera helianthoides*). In 1918 Blake presented the first monograph of the genus, including about 141 species (Blake 1918). Since then, many new species have been added to the genus, reaching up to 270 species distributed from the southwestern United States of America to Argentina in South America.

Schilling & Panero (2002, 2011) studied the subtribe Helianthinae based on molecular sequences of nuclear ITS, ETS, and cpDNA, stating that the genus *Viguiera* Kunth, as traditionally conceived, does not constitute a monophyletic group. Among their conclusions they propose to reclassify the genus, relocating its species in at least other nine genera: *Aldama* La Llave, *Bahiopsis* Kellogg, *Calanticaria* (B.L. Rob. & Greenm.) E.E. Schill. & Panero, *Davilanthus* E.E. Schill. & Panero, *Dendroviguiera* E.E. Schill. & Panero, *Gonzalezia* E.E. Schill. & Panero, *Heliomeris* Nutt., *Hymenostephium* Benth., *Sidneya* E.E. Schill. & Panero and *Viguiera* Kunth (Table 1).

The new classification of *Viguiera* reduces its number of species significantly, mainly restricted to South America. For North America (United States and Mexico), the genus includes two species (*Viguiera dentata* (Cav.) Spreng. and *V. moreliana* B.L. Turner (Turner 2015). Villaseñor (2016) reports for *Viguiera* nine species, but probably several of them are still not assigned to the genus to which they currently belong because they were not included in the molecular study that led to the reclassification of the *Viguiera* species. Future studies will certainly place them appropriately in the genus to which they belong.

Regarding the chemical studies of *Viguiera*, in 1985 the reports of the chemical compounds characterized from around 30 of the *ca.* 150 species included at that time in the genus (Romo de Vivar & Delgado 1985). Here we review the published secondary metabolites found in the 67 species were compiled reclassified in the nine genera segregated from *Viguiera*, according to the Schilling and Panero classification, and the biological activities for their extracts and secondary metabolites. The results allowed some chemotaxonomic observations and the analysis of the incidence of secondary metabolites between clades, which is discussed.

Materials and methods

The present study was accomplished by collecting the scientific data published on chemical compounds and biological activities of species of the genus *Viguiera sensu lato* between 1918 and 2021, using Scifinder, Scopus, Web of Science, and Google Scholar databases.

Results

Description of the chemical constituents. This section describes the main chemical constituents reported in the *Viguiera* species and species of the segregated genera. The studies have been carried out over the last decades, with varying methodologies and approaches. We detected chemical studies on 67 species (Appendixes 1-10) within the large *Viguiera* circumscription, and 322 secondary metabolites structurally characterized. Species of the genus *Viguiera s.l.* biosynthetize terpenoids represented mainly by sesquiterpene lactones (SLs) and diterpenes, although monoterpenes and triterpenes have also been found. Additionally, flavonoids, polyacetylenes, steroids, fatty acids and other hydroxylated and aromatic compounds are also reported.

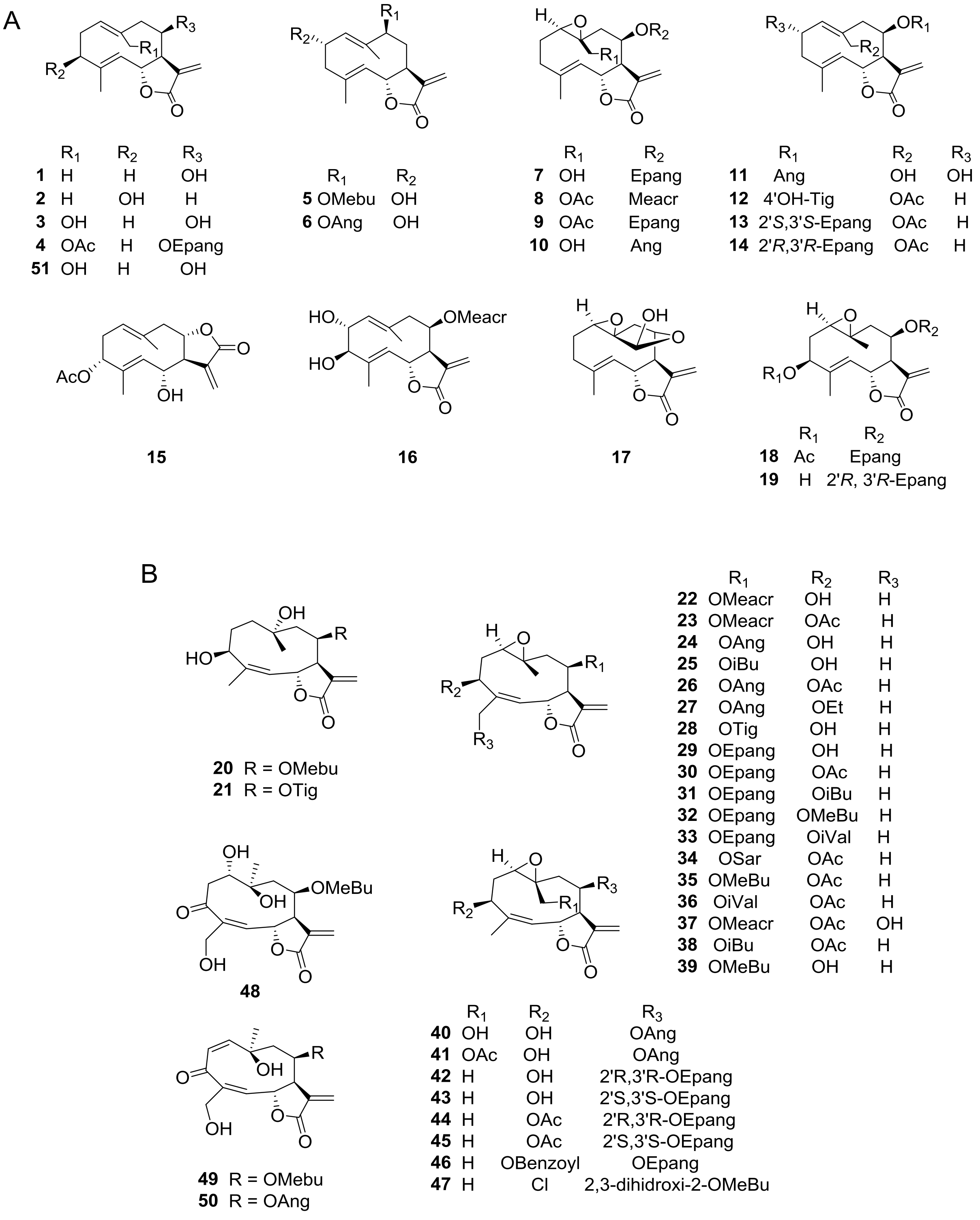
Sesquiterpene lactones (SLs) are major secondary metabolites in the Asteraceae family often used as chemotaxonomic markers (Da Costa *et al*. 2005); the Heliantheae tribe is rich in germacranolide-type compounds (Zdero & Bohlmann 1990). The characteristic SLs of the genus *Viguiera s. l.* have been reported in 35 of the 67 species studied and belong to the groups of germacrolides, heliangolides, furanoheliangolides, guaianolides, and eudesmanolides. Germacrolides (Figure 1A, **1-19**, **51**) have been reported in 12 species; heliangolides (Figure 1B, **20-50**) have been

Table 1. Genera included in the Subtribe Helianthinae (Tribe Heliantheae) of the family Asteraceae. An asterisk indicates the monophyletic genera derived from the new classification of the genus *Viguiera*. Abbreviations: CAME= Central America, MEX= Mexico, SAME= South America, USA= United States of America)

Genera	Total species	Distribution
**Aldama* La Llave, 1824	123	SW USA to SAME
**Bahiopsis* Kellogg, 1863	11	SW USA to MEX
**Calanticaria* (B.L. Rob. & Greenm.) E.E. Schill. & Panero, 2002	5	MEX
**Davilanthus* E.E. Schill. & Panero, 2010	7	MEX
**Dendroviguiera* E.E. Schill. & Panero, 2011	15	MEX to CAME
**Gonzalezia* E.E. Schill. & Panero, 2011	3	MEX
**Heiseria* E.E. Schill. & Panero, 2011	3	SAME
**Heliomeris* Nutt., 1848	6	NAME to MEX
**Hymenostephium* Benth., 1873	22	MEX to SAMEr
Iostephane Benth., 1873	4	MEX
Lagacea Cav., 1803	9	SW USA to SAME
Pappobolus S.F. Blake, 1916	37	SAME
Phoebanthus S.F. Blake, 1916	2	USA
Scalesia Arn., 1836	15	Galapagos Islands
Sclerocarpus Jacq., 1784	9	SW USA to SME, Old World
**Sidneya* E.E. Schill. & Panero, 2011	2	SW USA to MEX
Simsia Pers., 1807	29	SW USA to SAME
Syncretocarpus S.F. Blake, 1916	3	SAME
Tithonia Desf. ex Juss., 1789	12	SW USA to CAME
Viguiera Kunth, 1818	19	SW USA to SAME

isolated from 15 species; the most frequent compounds, furanoheliangolides (Figure 2A, **52-95**), have been found in 27 species; guaianolides (Figure 2B, **96-107**) in four species, and eudesmanolides (Figure 3A, **108-111**) in five species. The presence of a 1,10-epoxy group is observed in germacrolides (**7-10**, **17-19**) and in heliangolides (**22-47**). Most of them have an α-methylene 12,6-*trans* γ-lactone ring, except for **61** and **63**, isolated from *V. eriophora* (=*Aldama eriophora*) and *V. sylvatica* (=*Dendroviguiera sylvatica*), respectively, with a saturated γ-lactone, and those isolated from *V. deltoidea* (=*Bahiopsis deltoidea*) (**15**), from *V. pazensis* and *V. tucumanensis* (=*Aldama tucumanensis*) (**106** and **107**), and from *V. linearis* (=*Aldama linearis*) and *V. potosina* (=*Aldama canescens*) (**111**), with a C-8 lactone closure.

Diterpenes are also extensively distributed in the genus *Viguiera s.l.*, present in 39-out of 67 species studied. Acyclic diterpenoids are represented by six phytanes (Figure 3B, **112-117**) isolated from five species. Bicyclic diterpenoids have been isolated from seven species (Figure 3C, **118-124**), the *ent*-labdanes **118** and **119** were isolated from *V. robusta* (=*Aldama robusta*) and *V. stenoloba* (=*Sidneya tenuifolia*), respectively, **120-122** were found in *V. bishopii* (=*Aldama bishopii*) and **121** in *V. dentata*, *V. anchusifolia* (=*Aldama anchusifolia*), *V. pilosa* (=*Aldama pilosa*), and *V.* robusta (=*Aldama robusta*), and the *ent*-clerodanes **123-124**, were found in *V. tucumanensis* (=*Aldama tucumanensis*). Tricyclic diterpenoids have been isolated from seven species (Figure 4A): the abietane **125** was isolated from *V. procumbens* (*A. helianthoides*), the *ent*-pimaranes **126-132** and **137** from *V. arenaria* (=*Aldama arenaria*), **128** from *V. robusta* (=*Aldama robusta*), **133** from *V. pinnatilobata* (=*Sidneya pinnatilobata*), **134-136** from *V. discolor* (=*Aldama discolor*), and **138** from *V. anchusifolia* (=*Aldama. anchusifolia*) and *V. nudibasilaris* (=*Aldama nudibasilaris*). Tetracyclic diterpenes have been isolated from 32 species (Figure 4B), they are represented by *ent*-beyeranes (**139-147**), *ent*-kauranes (**148-184**, **192**), an *ent*-atisane **185**, and the villanovane **186**. The pentacyclic diterpenes *ent*-trachylobanes **187-191** have been found in five species (Figure 5A).



	R_1	R_2	R_3
1	H	H	OH
2	H	OH	H
3	OH	H	OH
4	OAc	H	OEpang
51	OH	H	OH

	R_1	R_2
5	OMebu	OH
6	OAng	OH

	R_1	R_2
7	OH	Epang
8	OAc	Meacr
9	OAc	Epang
10	OH	Ang

	R_1	R_2	R_3
11	Ang	OH	OH
12	4'OH-Tig	OAc	H
13	2'*S*,3'*S*-Epang	OAc	H
14	2'*R*,3'*R*-Epang	OAc	H

15

16

17

	R_1	R_2
18	Ac	Epang
19	H	2'*R*, 3'*R*-Epang

20 R = OMebu
21 R = OTig

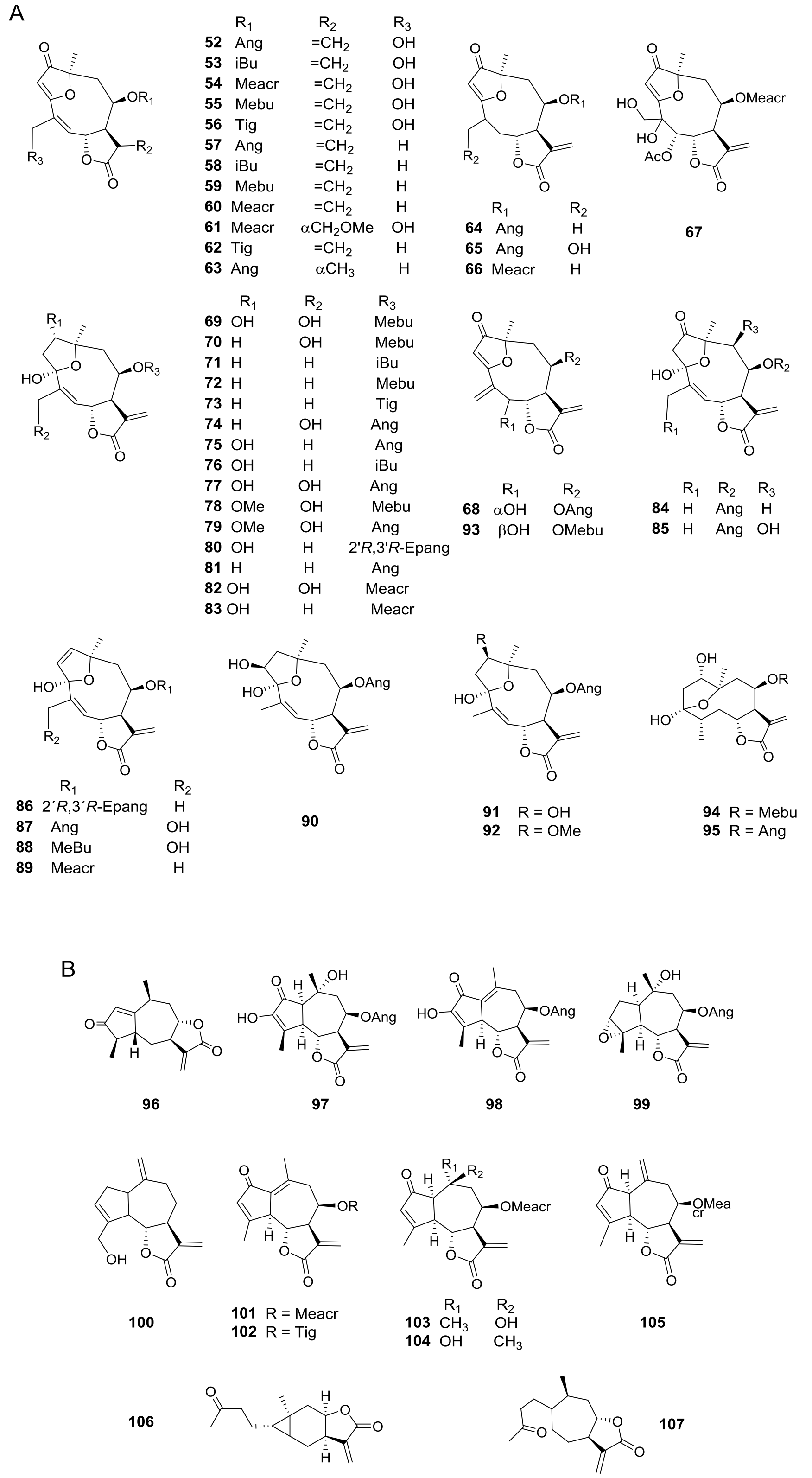
	R_1	R_2	R_3
22	OMeacr	OH	H
23	OMeacr	OAc	H
24	OAng	OH	H
25	OiBu	OH	H
26	OAng	OAc	H
27	OAng	OEt	H
28	OTig	OH	H
29	OEpang	OH	H
30	OEpang	OAc	H
31	OEpang	OiBu	H
32	OEpang	OMeBu	H
33	OEpang	OiVal	H
34	OSar	OAc	H
35	OMeBu	OAc	H
36	OiVal	OAc	H
37	OMeacr	OAc	OH
38	OiBu	OAc	H
39	OMeBu	OH	H

48

	R_1	R_2	R_3
40	OH	OH	OAng
41	OAc	OH	OAng
42	H	OH	2'R,3'R-OEpang
43	H	OH	2'S,3'S-OEpang
44	H	OAc	2'R,3'R-OEpang
45	H	OAc	2'S,3'S-OEpang
46	H	OBenzoyl	OEpang
47	H	Cl	2,3-dihidroxi-2-OMeBu

49 R = OMebu
50 R = OAng

Figure 1. A) Germacrolide-type sesquiterpene lactones from *Viguiera s. l.* species, B) Heliangolide-type sesquiterpene lactones from *Viguiera s. l.*



	R1	R2	R3
52	Ang	=CH$_2$	OH
53	iBu	=CH$_2$	OH
54	Meacr	=CH$_2$	OH
55	Mebu	=CH$_2$	OH
56	Tig	=CH$_2$	OH
57	Ang	=CH$_2$	H
58	iBu	=CH$_2$	H
59	Mebu	=CH$_2$	H
60	Meacr	=CH$_2$	H
61	Meacr	αCH$_2$OMe	OH
62	Tig	=CH$_2$	H
63	Ang	αCH$_3$	H

	R1	R2
64	Ang	H
65	Ang	OH
66	Meacr	H

	R1	R2	R3
69	OH	OH	Mebu
70	H	OH	Mebu
71	H	H	iBu
72	H	H	Mebu
73	H	H	Tig
74	H	OH	Ang
75	OH	H	Ang
76	OH	H	iBu
77	OH	OH	Ang
78	OMe	OH	Mebu
79	OMe	OH	Ang
80	OH	H	2'*R*,3'*R*-Epang
81	H	H	Ang
82	OH	OH	Meacr
83	OH	H	Meacr

	R1	R2
68	αOH	OAng
93	βOH	OMebu

	R1	R2	R3
84	H	Ang	H
85	H	Ang	OH

	R1	R2
86	2´*R*,3´*R*-Epang	H
87	Ang	OH
88	MeBu	OH
89	Meacr	H

91 R = OH
92 R = OMe

94 R = Mebu
95 R = Ang

101 R = Meacr
102 R = Tig

	R1	R2
103	CH$_3$	OH
104	OH	CH$_3$

Figure 2. A) Furanoheliangolide-type sesquiterpene lactones from *Viguiera s. l.* species, B) Guaianolide-type sesquiterpene lactones from *Viguiera s. l.*

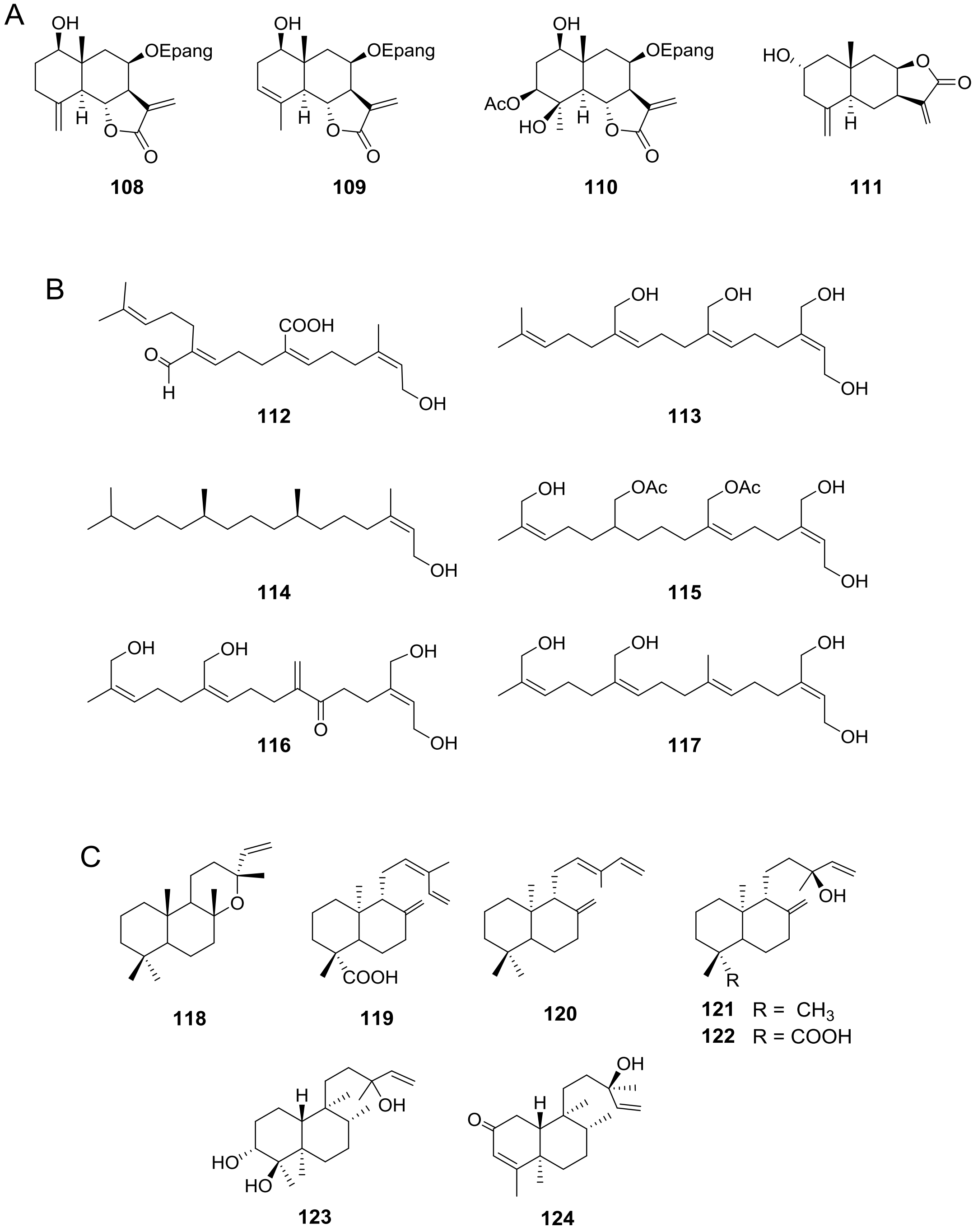
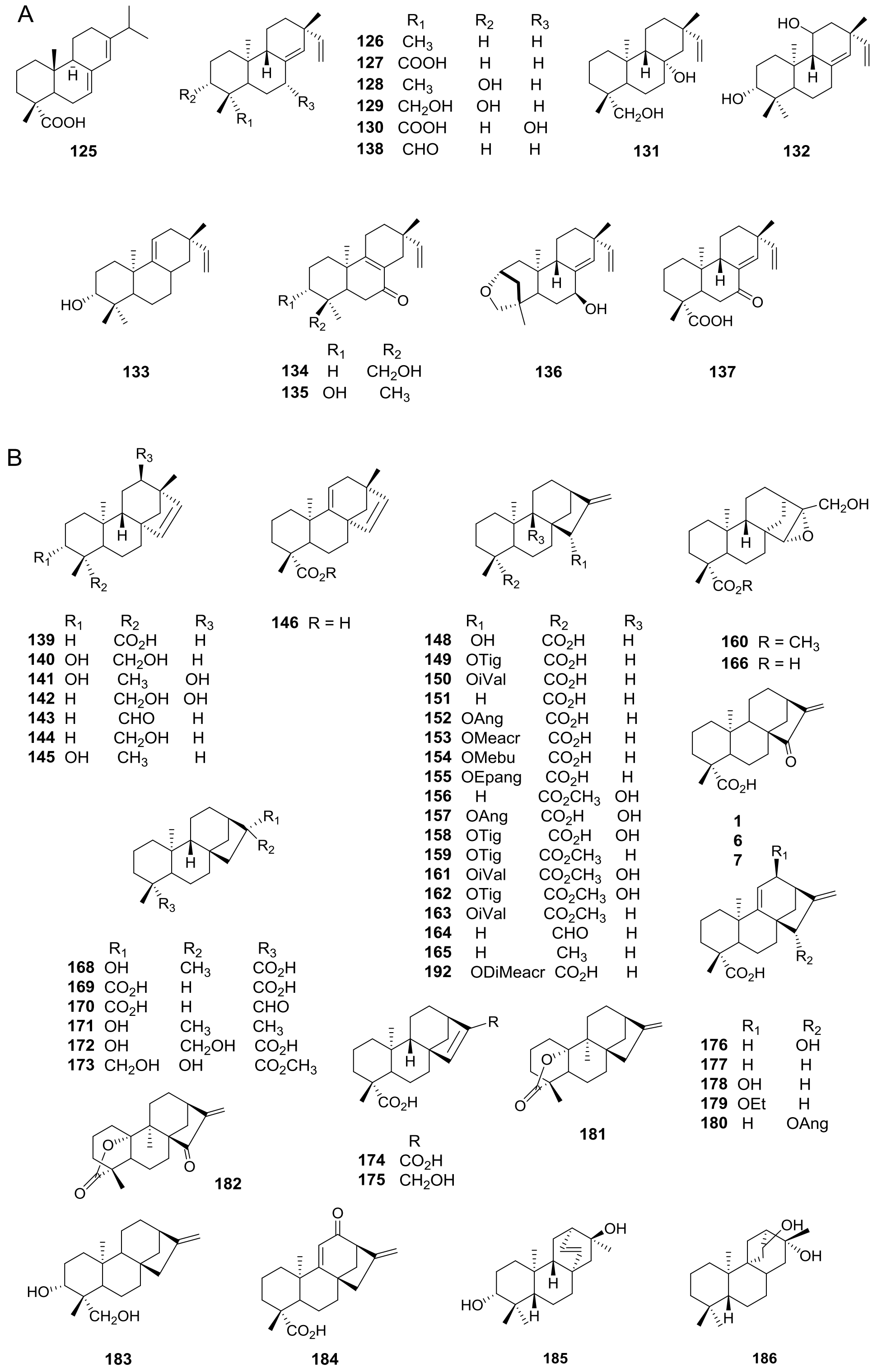


Figure 3. A) Eudesmanolide-type sesquiterpene lactones from *Viguiera s. l.* species, B) Acyclic diterpenoids in the genus *Viguiera s. l.*, 3C: Bicyclic diterpenoids in the genus *Viguiera s. l.*



	R_1	R_2	R_3
126	CH_3	H	H
127	COOH	H	H
128	CH_3	OH	H
129	CH_2OH	OH	H
130	COOH	H	OH
138	CHO	H	H

	R_1	R_2
134	H	CH_2OH
135	OH	CH_3

	R_1	R_2	R_3
139	H	CO_2H	H
140	OH	CH_2OH	H
141	OH	CH_3	OH
142	H	CH_2OH	OH
143	H	CHO	H
144	H	CH_2OH	H
145	OH	CH_3	H

146 R = H

	R_1	R_2	R_3
148	OH	CO_2H	H
149	OTig	CO_2H	H
150	OiVal	CO_2H	H
151	H	CO_2H	H
152	OAng	CO_2H	H
153	OMeacr	CO_2H	H
154	OMebu	CO_2H	H
155	OEpang	CO_2H	H
156	H	CO_2CH_3	OH
157	OAng	CO_2H	OH
158	OTig	CO_2H	OH
159	OTig	CO_2CH_3	H
161	OiVal	CO_2CH_3	OH
162	OTig	CO_2CH_3	OH
163	OiVal	CO_2CH_3	H
164	H	CHO	H
165	H	CH_3	H
192	ODiMeacr	CO_2H	H

160 R = CH_3
166 R = H

1
6
7

	R_1	R_2	R_3
168	OH	CH_3	CO_2H
169	CO_2H	H	CO_2H
170	CO_2H	H	CHO
171	OH	CH_3	CH_3
172	OH	CH_2OH	CO_2H
173	CH_2OH	OH	CO_2CH_3

	R
174	CO_2H
175	CH_2OH

	R_1	R_2
176	H	OH
177	H	H
178	OH	H
179	OEt	H
180	H	OAng

Figure 4. A) Tricyclic diterpenoids in the genus *Viguiera s. l.* species, B) Tetracyclic diterpenoids in the genus *Viguiera s. l.*

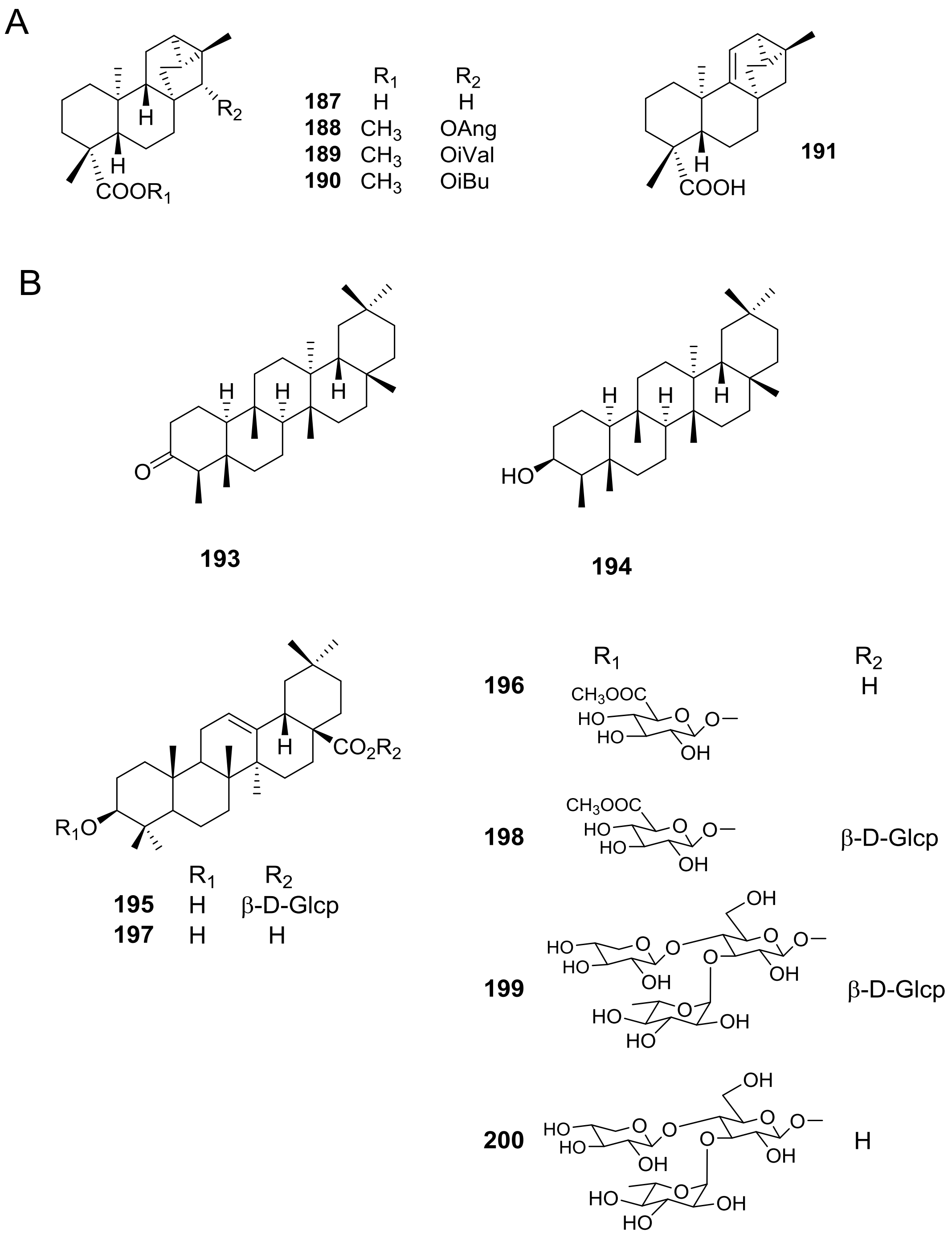


Figure 5. A) Pentacyclic diterpenoids in the genus *Viguiera s. l.* species, B) Pentacyclic triterpenoids in the genus *Viguiera s. l.*

Pentacyclic triterpenoids (Figure 5B) have been isolated from *V. decurrens* (=*Gonzalezia decurrens*) (**193-198**) and *V. hypargyrea* (=*Gonzalezia hypargyrea*) (**193-195**, **197-200**)*,* while the cycloartane hexacyclic triterpenoids (Figure 6A) **201-204** have been found in *V. dentata*, and **205** in *V. superaxillare* (=*Hymenostephium superaxillare*) (Appendixes 5 and 8).

Monoterpenoids (**206-219**) have been reported in essential oils. Non or low functionalized sesquiterpenoids (**220-243**) are also present in essential oils as well as in hexane extracts (Figure 6B).

Polyacetylenes (Figure 7A, **244-249**) were also found in *V. annua* (=*Heliomeris annua*), *V. procumbens* (=*Aldama helianthoides*), *V. incana* (=*Aldama incana*), *V. laceolata* (=*Aldama lanceolata*)*, V. oblonguifolia* (=*Aldama oblongifolia*)*, V. nervosa* (=*Aldama nervosa*)*, V. pazensis, and V. stenoloba* (=*Sidneya tenuifolia*) (Appendixes 1, 7, and 9).

Several studies on flavonoids content have been published as part of the systematic analysis of the series of *Viguiera* species included in Blake's (1918) revision of the genus. Initially, ultraviolet patterns were used to characterize the floral flavonoids involved in UV absorption among the species included in a taxonomic group (Reiseberg & Schilling 1985). In other studies, the flavonoid data were investigated to provide chemotaxonomic evidence on species relationships, both within the series and with other members of the genus (Schilling *et al.* 1988, Schilling & Panero 1988, Schilling 1989, Wollenweber *et al.* 1995). Flavonoids are represented by 46 structures isolated from 32 species (Figure 7B, Appendixes 1-5, 7, and 10), most of them are flavones (**250-254**, **258-266**, **271-273**, **279-284**) found in 27 species. There are also reports of ten flavonols present in 12 species (**267-270**, **274-278**, **285**), five of them glycosylated, seven chalcones (**286-292**); two aurones (**294**, **295**), three flavanones (**255-257**) isolated from *V. laciniata* (=*Bahiopsis laciniata*) and one flavanol (**293**) obtained from *V. quinqueradiata* (=*Dendroviguiera quinqueradiata*)*.* Other phenolic compounds such as benzofuran (**311**) and benzopyran derivatives (**296-299**, **306**, **307**, **310**, **312**), caffeic acid and some of its esters (**302-305**), and stilbenes (**308**, **309**) have been isolated (Figure 8A, Appendixes 1, 5, 7, and 10). Phytosterols (**313-315**), fatty acids (**316-318**), and phenyl alanine derivatives (**320-321**) have also been reported (Figure 8B).

Description of extracts and pure compounds with biological activity. The biological activities of extracts or pure compounds from 18 species of *Viguiera s.l.* have been reported (Table 2).

Trypanocidal activity.- The CH_2Cl_2 extracts of the Argentinean species *Aldama anchusifolia* and *A. tuberosa* were more active than the MeOH extracts of the same plants against *Trypanosoma cruzi*; results showed 82 and 93 % of growth inhibition, respectively, with 100 µg/mL of CH_2Cl_2 extract (benznidazole was used as positive control) (Selener *et al*. 2019). A trypanocidal activity research of pimarane diterpenes isolated from *Aldama arenaria* described the activity of the *ent*-15-pimarene-8ß,19-diol (**131**) with IC_{50} of 116.5 ± 1.21 µM while that of the positive control, gentian violet, was 76 **µ**M (Ambrosio *et al*. 2008). In other study *ent*-pimaradienoic acid (**127**) showed *in-vitro* trypanocidal activity with IC_{50} of 68.7 **µ**M (reference compound: benznidazole, IC_{50} = 9.8 ± 0.68 **µ**M), and the activity improved by esterification (Rocha *et al*. 2022). In vitro studies against *T. cruzi* identified the activity of compounds **151**, **171**, and **187** isolated from *Aldama aspilioides* (Da Costa *et al*. 1996a).

Insecticidal activity.- Phototoxic and insecticidal activities of polyacetylenes **244** and **245** isolated from *V. annua* (=*Heliomeris annua* (M.E. Jones) Cockerell) have been reported (Guillet *et al*. 1977). The insecticidal effect of saponins **195** and **198** isolated from *Gonzalezia decurrens* was evaluated on *Epilachna varivestis* larvae, these two saponines displayed activity with LC_{50} of 1380 and 80 mg/mol, respectively (Marquina *et al.* 2001). Clerodane **123** isolated from *Aldama tucumanensis* exhibited phytotoxicity against *Sorghum halepense* and *Chenopodium album*, and showed antifeedant activity (67 %) against *Epilachna palentulata* (Vaccarini *et al.* 1999, 2001).

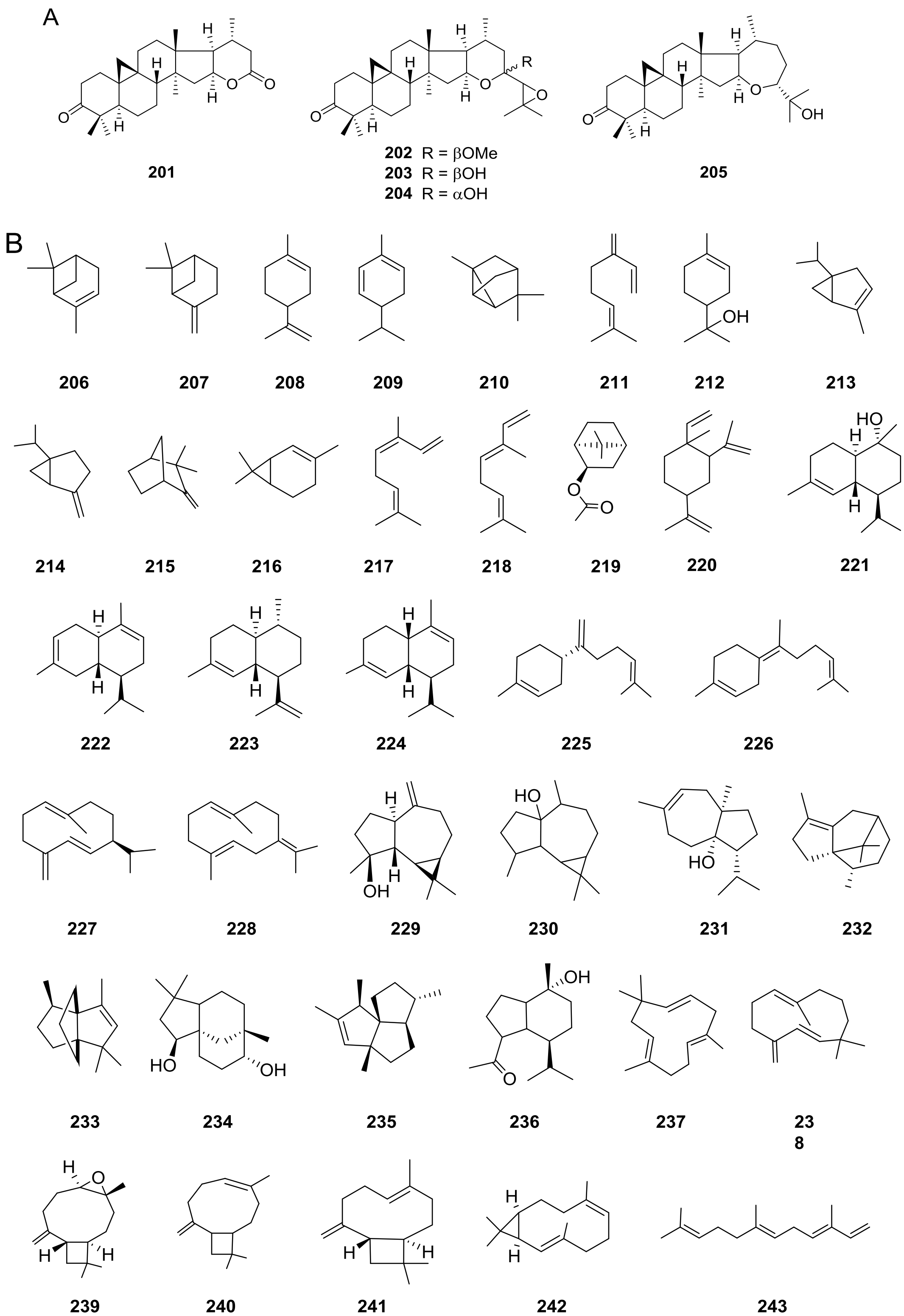
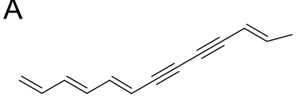
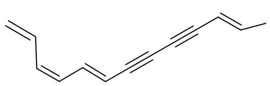


Figure 6. A) Hexacyclic triterpenoids in the genus *Viguiera s. l.* species, B) Volatile compounds obtained from *Viguiera s. l.* species.

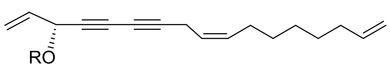
A



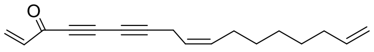
244



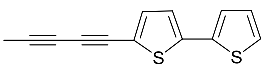
245



246 R = H
247 R = Ac

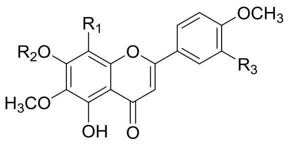


248

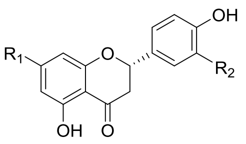


249

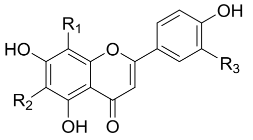
B



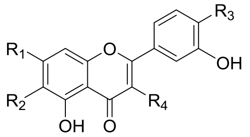
	R_1	R_2	R_3
250	H	CH_3	H
251	OCH_3	H	OH
252	OCH_3	H	H
253	OCH_3	H	OCH_3
254	H	H	OH



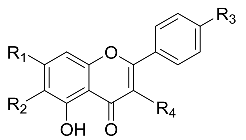
	R_1	R_2
255	OH	OCH_3
256	OCH_3	OCH_3
257	OH	H



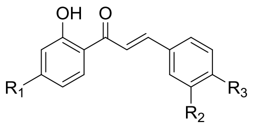
	R_1	R_2	R_3
258	H	H	OH
259	H	OCH_3	OH
260	H	OCH_3	H
261	OCH_3	OCH_3	OCH_3
262	OCH_3	H	OH
263	H	H	OCH_3
264	H	OCH_3	OCH_3
265	OCH_3	OCH_3	H



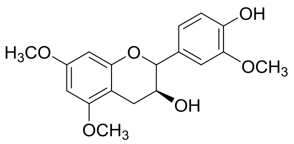
	R_1	R_2	R_3	R_4
266	OH	H	OCH_3	H
267	OGlc	H	OH	OH
268	OH	H	OH	OCH_3
269	OH	H	OH	OH
270	OH	OCH_3	OH	OCH_3
271	OCH_3	OH	OH	H
272	OCH_3	OCH_3	OH	H
273	OH	OH	OH	H
274	OH	H	OH	OGlc
275	OH	H	OH	OGal
276	OGlc	H	OH	OGlc
277	OH	OH	OH	OH
278	OGlc	OH	OH	OH



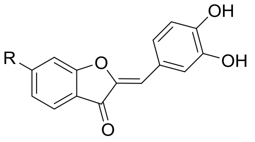
	R_1	R_2	R_3	R_4
279	OH	H	OH	H
280	OCH_3	OCH_3	OCH_3	H
281	OH	OCH_3	OCH_3	H
282	OCH_3	OH	OH	H
283	OCH_3	OH	OCH_3	H
284	OH	H	OCH_3	H
285	OH	H	OH	OCH_3



	R_1	R_2	R_3
286	OH	OH	OH
287	OGlc	OH	OH
288	OH	H	OCH_3
289	OH	H	OH
290	OGlc	H	OH
291	OCH_3	H	OH
292	OGlc	OCH_3	OH



293



294 R = OGlc
295 R = OH

Figure 7. A) Polyacetylenic compounds obtained from *Viguiera s. l* species. B) Flavonoids obtained from *Viguiera s. l.*

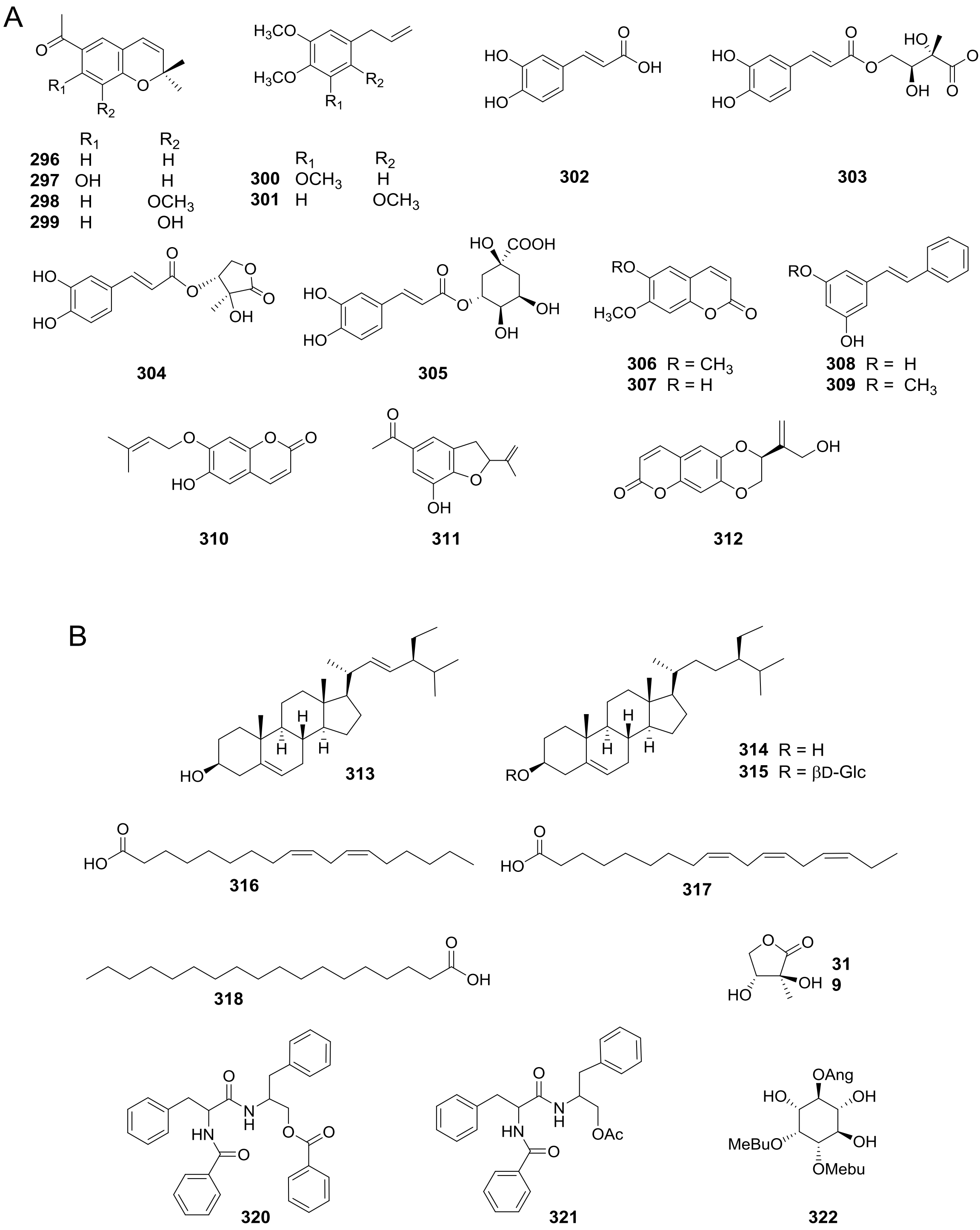


Figure 8. A) Other phenolic compounds obtained from *Viguiera s. l.* species, B) Other compounds obtained from *Viguiera s. l.*

Table 2: Biological activity of extracts and isolated compounds of the genus *Viguiera s.l.*

Species	**Activity**	**Extracts/Compounds**	**References**
V. anchusifolia Baker (=*Aldama anchusifolia* (DC.) E.E. Schill. & Panero)	Trypanocidal	MeOH, CH_2Cl_2	Selener *et al*. 2019
V. annua (M.E. Jones) Blake (=*Heliomeris annua* (M.E. Jones) Cockerell)	Phototoxic	**244**, **245**	Guillet *et al.* 1977
V. arenaria Baker (=*Aldama arenaria* (Baker) E.E. Schill. & Panero	Muscle relaxant	**127**	Ambrosio *et al*. 2002, Tirapelli *et al*. 2004
	Antimicrobial	**127, 128, 131**	Porto *et al.* 2009a, 2009b
		127, 151	Soares *et al.* 2019a, b
		127, **128**	Carvalho *et al*. 2011, Marangoni *et al.* 2018, Ferreira et al. 2018
	Trypanocidal	**131, 127**	Ambrosio *et al*. 2008, Rocha et al. 2022
	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas Paula *et al.* 2015
	Anti-inflammatory and analgesic	**127**	Possebon *et al*. 2014, Mizokami *et al*. 2016
	Antiproliferative activity	$CHCl_3$, **127, 128**	De Oliveira *et al*. 2021
	Genotoxic and anti- genotoxic effects	**127**	Kato *et al*. 2012
V. aspilioides Gardn. (=*Aldama aspilioides* (Baker) Schill. & Panero)	Trypanocidal	**151**, **171**, **187**	Da Costa *et al*. 1996[a]
	Antibacetrial	**187**	Da Costa et al. 1998
V. bracteata Gardner (=*Aldama bracteata* (Gardner) E.E. Schill. & Panero)	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas Paula *et al.* 2015
V. decurrens Gray (= *Gonzalezia decurrens* (A. Gray) E.E. Schill. & Panero)	Cytotoxic	Mixture of **195, 196**, **315**	Marquina *et al*. 2001
	Insecticidal	**195**, **198**	
V. dentata (Cav.) Spreng.	Antimicrobial	**151**, essential oil, hexane	Canales *et al*. 2008
	Antifungal	Hexane	
V. discolor Baker (= *Aldama discolor* (Baker) E.E. Schill. & Panero)	Antiprotozoal	CH_2Cl_2, and **134**, **183**	Nogueira *et al*. 2016
	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas-Paula *et al.* 2015
V. filifolia Sch. Bip. ex Baker (= *Aldama filifolia* (Sch. Bip. ex Baker) E.E. Schill. & Panero)	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas-Paula *et al*. 2015

Species	**Activity**	**Extracts/Compounds**	**References**
V. gardneri Baker (= *Aldama gardneri* (Baker) E.E. Schill. & Panero)	Anti-inflammatory	**101, 103, 104**	Schorr *et al*. 2002
V. hypargyrea (Greenm.) Blake (= *Gonzalezia hypargyrea* (Greenm.) E.E. Schill. & Panero)	Cytotoxic	**17**	Arellano-Martinez & Delgado 2010
	Spasmolytic	Hexane, **139**, **151**	Zamilpa *et al*. 2002
	Antimicrobial	**139**	
V. linearifolia Chodat. (= *Aldama linearifolia* (Chodat.) E.E. Schill. & Panero)	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas-Paula *et al*. 2015
V. pinnatilobata (Sch. Bip.) var. *megaphylla* (= *Sidneya pinnatilobata* (Sch. Bip.) E.E. Schill. & Panero var. *megaphylla* (Butterw. ex B.L. Turner) E.E. Schill. & Panero)	Spasmolytic	**133**	Campos-Lozada *et al*. 1993
V. robusta Gardn. (v= *Aldama radula* (Baker) E.E. Schill & Panero)	Analgesic		Arakawa *et al*. 2008
	anti-inflammatory	**52**	Valério *et al*. 2007, Nicolete *et al*. 2009.
	Analgesic, anti-inflammatory, anti-arthritic	**151**	Fattori *et al*. 2018, Zarpalon *et al.* 2017
	Inhibition of smooth muscle contractility	**127, 151**	Ambrosio *et al*. 2006 Tirapelli *et al.* 2002
	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas-Paula *et al*. 2015 Vasconcelos Faleiro *et al.* 2021
V. sylvatica Klatt (= *Dendroviguiera sylvatica* (Klatt.) E.E. Schill. & Panero)	Anti-inflammatory	**52**, **96**	Dupuy *et al.* 2008
	Cytotoxic		Taylor *et al*. 2008
V. trichophylla Dusén (= *Aldama trichophyla* (Dusén) Magenta)	Anti-inflammatory	EtOH-H_2O, MeOH-H_2O	Chagas-Paula *et al*. 2015, Vasconcelos Faleiro *et al.* 2021
V. tuberosa Griseb. (=*Aldama tuberosa* (Griseb.) E.E. Schill. & Panero)	Trypanocidal	MeOH, CH_2Cl_2	Selener *et al*. 2019
V. tucumanensis (Hook & Arn.) Griseb. (= *Aldama tucumanensis* (Hook. & Arn.) E.E. Schill. & Panero)	Phytotoxicity	**123**	Vaccarini *et al*. 1999
	Antifeedant		Vaccarini *et al*. 2001
	Cytotoxic	EtOH, **1, 24**	Gonzalez *et al*. 2018

Anti-spasmolytic and relaxant activities.- The relaxant action on rat thoracic aorta of pimaradienoic acid (**127**), isolated from *Aldama arenaria* as well as its effect on the contraction of carotid rings were demonstrated (Ambrosio *et al*. 2002, Tirapelli *et al*. 2004). The effect on the inhibition of smooth muscle contractility by different concentrations of *ent*-kaurenoic acid (**151**) isolated from *Aldama robusta* was documented (Tirapelli *et al*. 2002). Diterpenes **127** and **151** inhibited vascular contractility mainly by blocking the extracellular Ca^{2+} influx (Ambrosio *et al*. 2006). The hexane extract of *Gonzalezia hypargyrea* showed spasmolytic activity, this activity was attributed to beyerenoic acid (**139**) by the inhibition of the electrically induced contractions of guinea pig ileum by 63.64 ± 6.1 %, with ED_{50} of 4.9 µg/ml (the positive control, papaverine showed inhibition of 82.8 ± 2.1 %) (Zamilpa *et al*. 2002). The spasmolytic effect of viguiepinol (**133**) obtained from *V. pinnatilobata* (=*Sidneya pinnatilobata*) was demonstrated *in-vitro* (Campos-Lozada *et al*. 1993).

Antimicrobial activity.- Dichloromethane extract of roots of *Aldama arenaria* and the isolated *ent*-pimarane derivatives **127**, **128**, and **131**, displayed activity against gram-positive bacteria, showing the highest activities against *Streptococcus agalantiae, S. dysgalantiae* and *Staphylococcus epidermis,* with MIC values between 3.31 and 16.31 µM (vancomycin hydrochloride, used as positive control, showed MIC values between 0.34 and 0.47 µM); these compounds were also active against microorganisms responsible for dental caries with MIC values between 7.8 and 20.8 µM (chlorhexidine dihydrochloride, the positive control, showed MIC values between 0.16 and 0.64 µM) (Porto *et al*. 2009a, b). In other study, diterpene **127**, isolated from *V. arenaria* was tested against clinically isolated gram-positive multi-resistant bacteria, and the results indicated that this compound was a promising antibacterial agent (Soares *et al*. 2019a, b). Compounds **127** and **128** showed activities against endodontic bacteria (Carvalho *et al*. 2011, Marangoni *et al*. 2018, Ferreira et al. 2018). The antibacterial activity of *ent*-traquilobanic acid (**187**), isolated from *A. aspillioides*, was tested against several gram positive bacteria showing the highest activity against *S. aureus* and *S. epidermis* (MIC 7.8 µg/ml, the positive control used in the screening phase was gentamicine) (Da Costa *et al*.1998). The antimicrobial activity of *V. dentata*'s essential oil, hexane extract, and **151**, as well as the activity of the hexane extract was pointed out (Canales *et al*. 2008). Beyerenoic acid (**139**), isolated from *Gonzalezia hypargyrea*, inhibited the growth of *Staphylococcus aureus* and *Enterococcus faecalis* with a MIC of 12 µg/ml for each of them, using gentamicin as positive control (MIC 0.8 µg/mL) (Zamilpa *et al.* 2002).

Anti-inflammatory activity.- EtOH-H_2O and MeOH-H_2O extracts of *Aldama arenaria*, *A. bracteata, A. discolor*, *A. filifolia, A. linearifolia, A. robusta,* and *A. trichophylla* showed anti-inflammatory action through the inhibition of cyclooxygenase-1 (COX-1) and 5-lipoxygenase (5-LOX) (Chagas-Paula *et al*. 2015). A study on leaf extracts of 22 *Aldama* species, using LC – MS metabolomics and in vitro enzymatic assays to indentify COX-1 and 5-LOX inhibitors, showed that *A. robusta* and *A. trichophylla* inhibited these two key enzymes (Vasconcelos Faleiro *et al.*). Pimaradienoic acid (**127**), from *A. arenaria*, showed anti-inflammatory effect in carrageenan-induced inflammation by reducing oxidative stress, nitric oxide, and cytokine production (Mizokami *et al*. 2016). The analgesic effects of diterpene **127** were demonstrated and associated with the inhibition of the NF-κB factor activation, reduction of cytokine production, and activation of the NO–cyclic GMP–protein kinase G-sensitive potassium signaling pathway (Possebon *et al*. 2014). Guaianolides **101**, **103**, **104**, isolated from *Aldama gardneri*, showed anti-inflammatory activity inhibiting the transcription factor NF-κB (Schorr *et al*. 2002). Budlein A (**52**), isolated from *Aldama robusta* showed anti-inflammatory activity by the inhibition of inflammatory mediator release and neutrophil migration (Arakawa *et al*. 2008; Nicolete *et al*. 2009, Valério *et al*. 2007), inhibited the antigen-induced arthritis in mice and pain by targeting the NF-κB factor, does not induce in vivo side effects (Zarpelon *et al*. 2017), and reduced mechanical hypersensibility, knee joint edema pain and inflammation in a model of acute gout arthritis in mice (Fattori *et al*. 2018). SLs **52** and **96**, isolated from *Dendroviguiera sylvatica* inhibited the nitric oxide production and phagocytosis of macrophages (Dupuy *et al*. 2008).

Genotoxic activity.- Pimaradienoic acid **127**, isolated from *A. arenaria*, was studied for its *in vitro* and *in vivo* genotoxic and anti-genotoxic effects. *In vitro* results showed that **127** induces DNA damage at concentrations between 2.5 and 5.0 µg/mL, and in the *in vivo* evaluation of genotoxicity a significant damage was observed in the hepatocites of animals treated at 80 mg/Kg, compared with the control group (Kato *et al*. 2012).

Cytotoxic activity.- The $CHCl_3$ extract of roots of *A. arenaria* and some fractions were evaluated in vitro for their antiproliferative activity against 10 tumor cell lines. The extract showed weak to moderate antiproliferative activities, while fractions enriched with diterpenes **127** and **128** presented moderate to potent activities in most of tested cell lines (de Olveira *et al*. 2021). The mixture of compounds **195**, **196**, and **315**, isolated from *Gonzalezia decurrens*, showed cytotoxic activity against murine lukemia (ED_{50} 2.3 µg/mL); however, the pure compounds were not active (Marquina *et al*. 2001). Hypargyrin A (**17**), a germacrolide from *Gonzalezia hypargyrea* showed mild activity against HeLa (cervical) and Hep-2 (larynx) cell lines, reported activities were IC_{50} 35.1 ± 2.7 µM (positive control: 5-fluoro-uracil IC_{50} 1.5 ± 0.19 µM) and IC_{50} 39.2 ± 3.1 µM (positive control: 5-fluoro-uracil IC_{50} 1.0 ± 0.17 µM), respectively; compound **17** displayed also a modest anti-inflammatory effect (Arellano-Martínez & Delgado 2010). The antiproliferative properties of SLs **52** and **96**, isolated from *V. sylvatica* (=*Dendroviguiera sylvatica*), against cell lines in vitro and on the growth of melanoma tumors in mice were examined, results showed cytotoxicity *in vitro* and antitumor activity *in vivo* for SLs 52 (Taylor *et al*. 2008). Ethanol extract from *V. tucumanensis* (=*Aldama tucumanensis*) exhibited cytotoxic activity and two of its components, leptocarpin (**24**) and eupatolide (**1**), have shown significant cytotoxic properties (González *et al*. 2018).

Discussion

Comments on the biological activity of the secondary metabolites found in Viguiera s.l. The published biological activities of the secondary metabolites of *Viguiera s.l.* are but a tiny sample of the potential activities of those compounds; those activities reflect the interest of the researchers that assayed the metabolites. A common secondary metabolite trait is the ability to affect several physiological targets (Maffei *et al*. 2011, Hu & Bajorath 2013). Therefore, the biological activity of a secondary metabolite is usually multifunctional (Langenheim 1994; Gershenzon & Dudareva 2007), *i.e*., it can display activity on many wild species, pathogens or pathological processes in humans, as shown by Torres-Gurrola *et al.* (2016) with 364 secondary metabolites found in *Persea americana*.

On the relevance of phytochemical studies in Asteraceae. Phytochemical data are helpful to solve some taxonomic problems or for reinforcing certain phylogenetic relationships. Numerous publications highlight their taxonomic and ecological importance (for example, Seigler & Price 1976). In particular for the Asteraceae family, there are relevant publications on this topic, such as the results of symposia on the Biology and Chemistry of the Compositae (Heywood *et al*. 1977, Hind & Beentje, 1996), the contributions on its flavonoid content (Bohm & Stuessy 2001, Emerenciano *et al*. 2001), on its diterpenes and sesquiterpenes (Seaman 1982, Seaman *et al.* 1990, Spring & Buschmann 1996), and on its sesquiterpene lactones (Zidorn 2008, Shulha & Zidorn 2019). Especially noteworthy for Mexico are the summaries on the studies of secondary metabolites in the species of *Viguiera* and in species of the tribe Senecioneae (Romo de Vivar & Delgado *et al*. 1985, Romo de Vivar *et al.* 2007).

Figure 9 shows the placement of the species of *Viguiera s.l.* with chemical constituents' reports following the phylogenetic relationships proposed by Schilling & Panero (2002, 2011). Nondistinctive patterns are observed between clades and chemical groups because all segregated genera share most main secondary metabolites (Appendixes 1-10), some of them more frequent than others in certain clades.

The commonest secondary metabolites among the studied species are the flavonoids, followed by the tetracyclic diterpenoids and the furanoheliangolide-type sesquiterpene lactones. The chemical variants of each one has been recorded for the species (Appendixes 1-10), reaching a figure of 322 different secondary metabolites in just 67 species, an average of 5 per species.

There is a close relationship between certain clades indicated in Figure 9 with the classification proposed by Blake (1918). See Table S1. For example, most North American taxa included in his Subgenus *Amphilepis* now belong to different monophyletic genera. In this way, species of the genus *Bahiopsis* Kellogg are included in his Series *Dentatae*, the genus *Calanticaria* (B.L. Rob. & Greenm.) E.E. Schill. & Panero in his Series *Brevifolia*, the genus *Gonzalezia* E.E. Schill. & Panero corresponds to his Section *Hypargyrea* (Subgenus *Amphilepis*), or the genus *Sidneya* E.E. Schill. & Panero to his Series *Pinnatilobatae*. Table S1 includes the species with phytochemical studies arranged following the Blake´s classification.

Chemotaxonomic observations. The secondary metabolites present in *Viguiera s.l.* species are terpenoids, polyacetylenes, flavonoids, phenols, and others. As previously noted, sesquiterpene lactones, polycyclic diterpenes, and flavonoids are the major groups of secondary metabolites in *Viguiera s.l.* species. Therefore, to compare the metabolic content among the segregated genera, the SLs and polycyclic diterpenes were divided according their biogenetic complexity and / or structural type, as shown in figures 10A and 10B. Sesquiterpene lactones are biosynthesized from germacryl cation to germacrolides (*i.e*., budlein B), which is closely related to heliangolides (*i.e*., deacetylviguiestenin) and the formation of the C3-C10 epoxide affords the furanoheliangolides (*i.e*., budlein A). Cyclization of germacrolides produces eudesmanolides, while the 4,5-epoxy-germacrolides (*i.e*., parthenolide) are the precursors of guaianolides. Thus, sesquiterpene lactones were divided in five groups: germacrolides (GERM), heliangolides (HELI), furanoheliangolides (FUHE), guaianolides (GUAI) and eudesmanolides (EUDE). See figure 10A.

Geranyl pyrophosphate is considered the direct precursor of linear (acyclic) diterpenes, and cyclization of this compound affords the bicyclic copalyl-pyrofosfate, which in turn produces tricyclic compounds (*i.e*., abietane and labdane diterpenes). Cyclization of the labdane diterpenes affords tetracyclic *ent*-beyerane and *ent*-kaurane diterpenes. Additional cyclization of tetracyclic diterpenes produces pentacyclic diterpenes (*i.e*. trachylobanoic acid). Diterpenes were divided in acyclic and bicyclic diterpenes (ABID), tri- (TRID), tetra- (TETD) and pentacyclic diterpenes (PEND). See figure 10B.

Table 3 provides an overview about the occurrence of different types of secondary metabolites reported per each species (distributed in *Viguiera* and its segregated genera).

Observations on the incidence of the secondary metabolites of Viguiera s.l. *species.* According to the data shown in Appendixes 1-10 and table 3, twenty five out of 31 *Aldama* species with chemical studies deal on the constituents of the aerial parts, and these report sesquiterpene lactones and tetracyclic triterpenes (entries 2, 3, 5-8, 10,11, 13-24, 26, 28, 29, 30, 31 of Table 3) as the main constituents. The 95 SLs reported for 20 *Aldama* species include 50 furanoheliangolides, 19 heliangolides, 16 germacrolides, seven guaianolides and three eudesmanolides. The roots and / or the essential oils were chemically investigated for 16 *Aldama* species (entries 1, 3-5, 9, 12, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30 of Table 3). For *Aldama* species, it is evident that furanoheliangolides (FUHE) and tetracyclic diterpenes (TETD) are the prevalent chemical groups in the leaves.

Chemical analysis of the leaves of three species of *Bahiopsis* (entries 33, 34, 36 of Table 3) afforded sesquiterpene lactones of several types (GERM, HELI, FUHE, GUAI, EUDE). Almost all species of this genus contain flavonoids (FLAV).

Furanoheliangolides (FUHE) and tetracyclic diterpenes (TETD) have been informed as constituents of the aerial parts of *Calanticaria greggi*, in addition to the flavonoids (FLAV) in the three species (entries 42-44).

The flavonoid chemistry of *Dendroviguiera* species (entries 45-55) was discussed previously, considering that this group was part of the Section Maculatae of the *Viguiera* genus *s.l.* (Schilling & Panero 1988). Germacrolides (GERM), heliangolides (HELI) and furanoheliangolides (FUHE) and tetracyclic diterpenes (TETD) have been characterized from *Dendroviguiera* species. A high infraspecific diversity in the chemical constituents has been noted in this group (considering the less abundant presence of 1-keto-2,3-unsaturated furanoheliangolides), and it has been suggested that the lack of SLs in some species (entries 47 and 49 of Table 3) may be related to the absence of glandular trichomes (Spring *et al*. 2000).

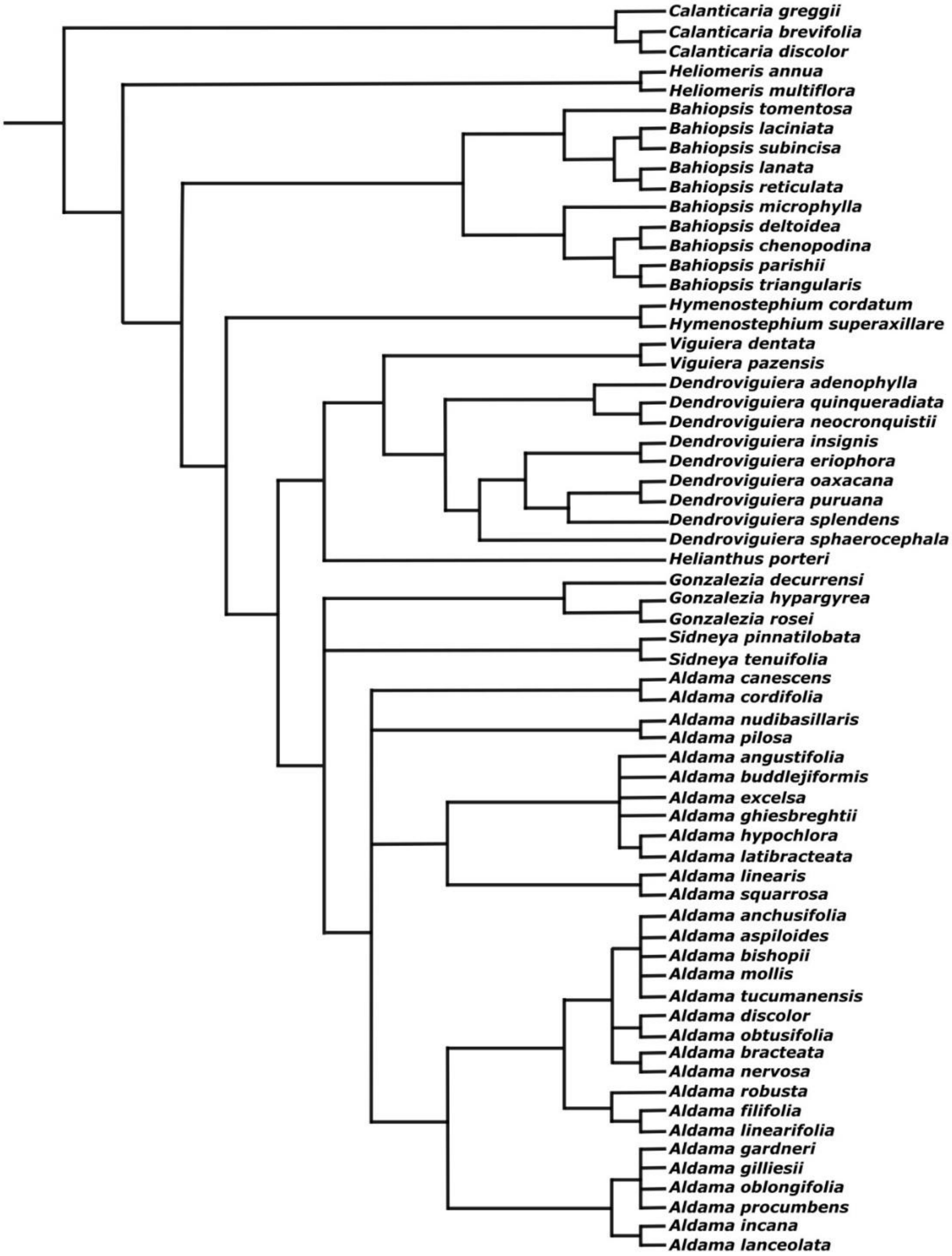


Figure 9. Cladogram illustrating the phylogenetic relationships between *Viguiera* species and segregated genera (*Viguiera s. l.*) with phytochemical studies discussed in this work (Adapted from Schilling & Panero (2002, 2011)).

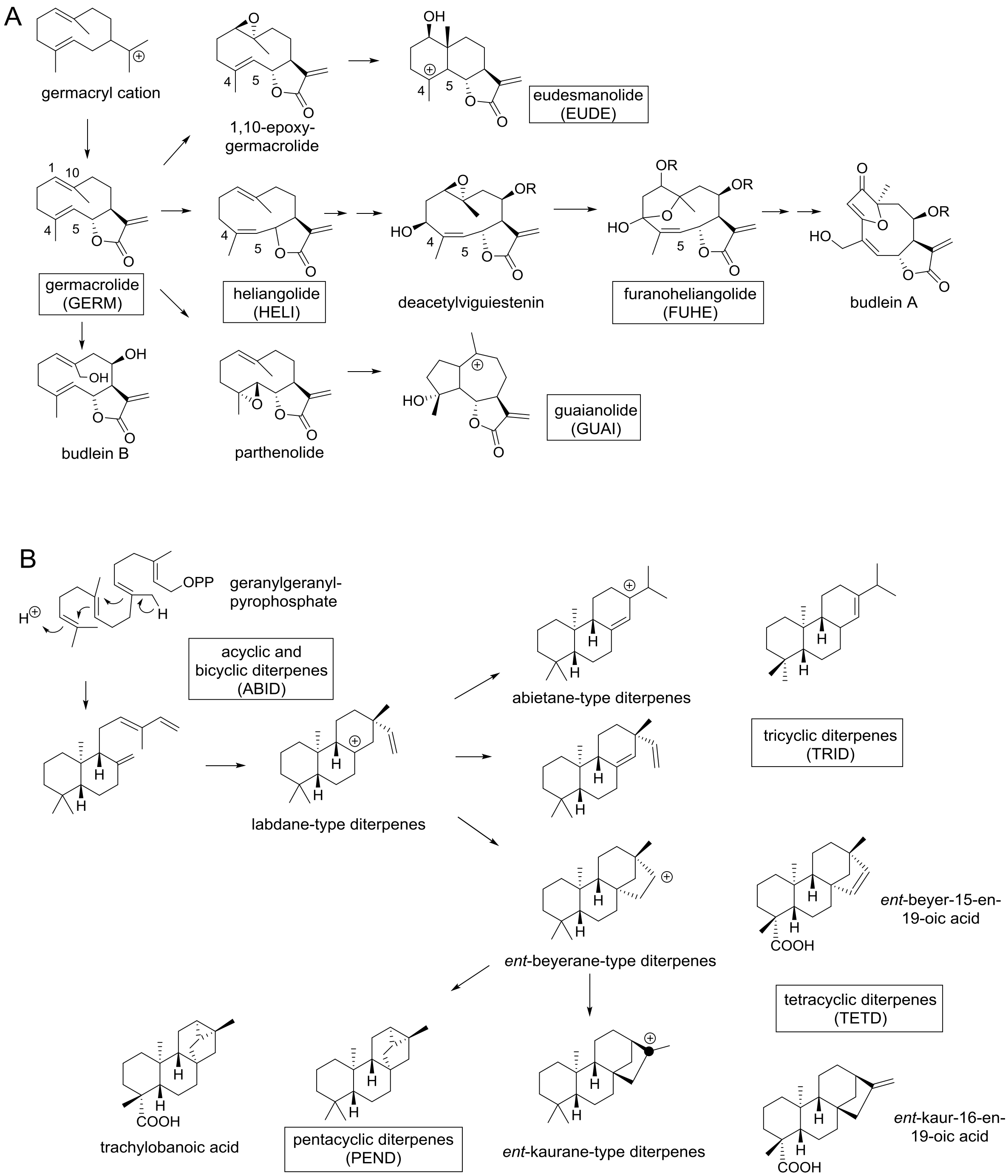


Figure 10. A) Biogenetic relationships of the major type of sesquiterpene lactones found in *Viguiera s. l.* species and their acronyms, B) Biogenetic relationships of the major type of diterpenes found in *Viguiera s. l.* species and their acronyms.

Table 3. Distribution of the occurrence of secondary metabolites in the new genera / species segregated from *Viguiera.* Germacrolides (GERM), heliangolides (HELI), furanoheliangolides (FUHE), guaianolides (GUAI), eudesmanolides (EUDE), acyclic plus bicyclic diterpenes (ABID), tri- (TRID), tetra- (TETD), penta- cyclic (PEND) diterpenes, pentacyclic triterpenes (PENT), and flavonoids (FLAV).

Species	GERM	HELI	FUHE	GUAI	EUDE	ABID	TRID	TETD	PEND	PENT	FLAV
1 *Aldama anchusifolia*	0	0	0	0	0	1	1	0	0	0	0
2 *Aldama angustifolia*	0	0	1	0	0	0	0	0	0	0	0
3 *Aldama arenaria*	0	0	1	0	0	0	8	0	0	0	0
4 *Aldama aspilioides*	0	0	0	0	0	0	0	8	1	0	0
5 *Aldama bishopii*	0	0	0	0	0	3	0	5	2	0	0
6 *Aldama bracteata*	2	3	10	0	0	0	0	0	0	0	0
7 *Aldama buddleiajiformis*	1	0	1	0	0	0	0	4	0	0	3
8 *Aldama canescens*	0	0	0	0	1	0	0	4	0	0	0
9 *Aldama cordifolia*	0	0	0	0	0	0	0	2	0	0	0
10 *Aldama discolor*	0	0	1	0	0	0	3	1	0	0	0
11 *Aldama excelsa*	0	0	1	0	0	0	0	6	0	0	0
12 *Aldama filifolia*	0	0	0	0	0	0	0	0	0	0	0
13 *Aldama gadneri*	1	0	0	5	0	0	0	0	0	0	2
14 *Aldama gilliesii*	0	2	3	0	0	1	0	0	0	0	0
15 *Aldama ghiesbreghtii*	0	0	1	0	0	0	0	0	0	0	0
16 *Aldama helienthoides*	2	3	4	0	0	2	1	2	1	0	1
17 *Aldama hypochlora*	0	0	1	0	0	0	0	0	0	0	0
18 *Aldama incana*	0	0	0	0	0	0	0	1	0	0	0
19 *Aldama lanceolata*	0	0	1	0	0	0	0	1	1	0	0
20 *Aldama latibracteata*	0	0	2	0	0	0	0	12	0	0	0
21 *Aldama linearifolia*	0	0	0	0	0	0	0	1	0	0	0
22 *Aldama linearis*	2	4	7	0	1	0	0	4	0	0	0
23 *Aldama mollis*	0	0	2	0	0	0	0	0	0	0	2
24 *Aldama nervosa*	0	0	0	0	0	0	0	3	0	0	0
25 *Aldama nudibasilaris*	0	0	0	0	0	0	1	1	0	0	0
26 *Aldama oblongifolia*	0	0	2	0	0	0	0	0	0	0	0
27 *Aldama pilosa*	0	0	0	0	0	1	0	0	0	0	0
28 *Aldama robusta*	7	4	8	0	1	2	1	8	0	0	0
29 *Aldama squarrosa*	0	0	1	0	0	0	0	0	0	0	0
30 *Aldama trichophyla*	0	0	0	0	0	0	0	3	0	0	0
31 *Aldama tucumanensis*	1	3	3	2	0	2	0	1	0	0	0
32 *Bahiopsis chenopodina*	0	0	0	0	0	0	0	0	0	0	6
33 *Bahiopsis deltoidea*	1	0	2	0	0	1	0	0	0	0	7
34 *Bahiopsis laciniata*	0	7	0	0	1	1	0	0	0	0	9

Species	**GERM**	**HELI**	**FUHE**	**GUAI**	**EUDE**	**ABID**	**TRID**	**TETD**	**PEND**	**PENT**	**FLAV**
35 *Bahiopsis lanata*	0	0	0	0	0	0	0	0	0	0	4
36 *Bahiopsis microphylla*	1	0	2	0	0	0	0	0	0	0	5
37 *Bahiopsis parishii*	0	0	0	0	0	0	0	0	0	0	2
38 *Bahiopsis reticulata*	0	0	0	0	0	0	0	0	0	0	3
39 *Bahiopsis subincisa*	0	0	0	0	0	0	0	0	0	0	3
40 *Bahiopsis tomentosa*	0	0	0	0	0	0	0	0	0	0	3
41 *Bahiopsis triangularis*	0	0	0	0	0	0	0	0	0	0	8
42 *Calanticaria bicolor*	0	0	0	0	0	0	0	0	0	0	10
43 *Calanticaria brevifolia*	0	0	0	0	0	0	0	0	0	0	9
44 *Calanticaria graggi*	0	0	3	0	0	0	0	2	0	0	15
45 *Dendroviguiera adenophylla*	0	0	0	0	0	0	0	0	0	0	11
46 *Dendroviguiera eriophora*	0	3	6	0	0	0	0	3	0	0	14
47 *Dendroviguiera insisgnis*	0	0	0	0	0	0	0	10	0	0	0
48 *Dendroviguiera neocronquistii*	0	0	0	0	0	0	0	0	0	0	4
49 *Dendroviguiera oaxacana*	0	0	0	0	0	0	0	2	0	0	4
50 *Dendroviguiera pringlei*	0	0	0	0	0	0	0	0	0	0	11
51 *Dendroviguiera puruana*	1	11	0	0	1	0	0	0	0	0	3
52 *Dendroviguiera quinqueradiata*	0	2	1	0	0	0	0	2	0	0	9
53 *Dendroviguiera sphaerocephala*	1	1	0	0	0	0	0	0	0	0	13
54 *Dendroviguiera splendens*	0	0	0	0	0	0	0	0	0	0	6
55 *Dendroviguiera sylvatica*	0	1	8	4	0	2	0	1	0	0	0
56 *Gonzalezia decurrens*	0	0	0	0	0	0	0	2	0	6	2
57 *Gonzalezia hypargyrea*	7	0	0	0	0	0	0	5	0	7	3
58 *Gonzalezia rosei*	0	0	0	0	0	0	0	0	0	0	5
59 *Helianthus porteri*	0	0	0	0	0	0	0	7	0	0	0
60 *Heliomeris annua*	0	0	0	0	0	0	0	0	0	0	0
61 *Heliomeris multiflora*	0	0	0	0	0	0	0	0	0	0	5
62 *Hymenostephium cordatum*	0	0	4	0	0	0	0	1	0	0	0
63 *Hymenostephium superaxillare*	0	0	0	0	0	0	0	3	0	0	0
64 *Sidneya pinnatilobata*	0	2	1	0	0	0	1	0	0	0	0
65 *Sidneya tenuifolia*	0	2	0	0	0	1	0	9	0	0	0
66 *Viguiera dentata*	0	0	1	0	0	1	0	9	1	4	0
67 *Viguira pazensis*	0	1	2	1	0	0	0	7	4	0	2

In addition to flavonoids (FLAV), tetracyclic ditepenes (TETD) and pentacyclic triterpenes (PENT) have been characterized in *Gonzalezia*. The members of *Gonzalezia* were recognized as a monophyletic group (Wollenweber *et al*. 1995). It is noteworthy that exclusively germacrolides (GERM) have been characterized from the aerial parts of *G. hypargyrea* (Álvarez *et al*. 1985, Arellano & Delgado 2010).

Heliangolides (HELI), furanoheliangolides (FUHE) and bi- and tetracyclic diterpenes are the main constituents of *Sidneya.*

To explore if the species segregated from *Viguiera* grouped according to the secondary metabolites found in those species, we performed a cluster analysis with four types of sesquiterpene lactones and bi-, tri-, and tetraterpenoids and the 38 species remaining after eliminating those that had no sesquiterpene lactones and those terpenoids (Figure 11).

The species grouping does not coincide with the phylogenetic clusters shown in Figure 9. In many cases, species classified closely belong to different genera, and the species in the same genus were classified away from their congeneric species. We do not have the certainty that all the secondary metabolites analyzed in Figure 11 used were searched and detected in all species. However, the absence of correlation between the phylogenetic and phytochemical classifications is consistent with a similar comparison made with *Jacobaea* species and their pyrrolizidine alkaloids, where the authors concluded that the distribution of the alkaloids was determined by ecological factors (Chen *et al*. 2022). Thus, we suggest that the sesquiterpene lactones and diterpenes characterized until now are not sufficiently informative as chemotaxonomic markers to make clear distinctions between the segregated genera from *Viguiera*.

Theoretical or methodological assumptions can explain the lack of distinctive chemotaxonomic patterns among *Viguiera s.l.* One is the lack of certainty that all species have been studied in the same way; for example, the studies of Schilling et al. (1988) or Schilling & Panero (1988) focused on the study of flavonoids, considerably increasing the number of species studied in this particular type of compounds, many of them poorly or never studied in search of other compounds. Other studies focused mainly on SLs, avoiding the search for other compounds. Furthermore, intraspecific phytochemical variation is a generalized phenomenon found in diurnal, seasonal variations, by the attack of herbivores or pathogens, and by ontogeny of tissues or individuals. In addition, there is also variation within and between individuals and populations (García-Rodríguez *et al.* 2012, Espinosa-García *et al*. 2021). Furthermore, perhaps for several *Viguiera s.l.* species the biosynthetic route for several metabolites has been lost or blocked against other more ecologically fruitful compounds, however, the test to probe the latter rarely is assessed.

In conclusion, the review of the natural products structurally characterized from *Viguiera* species and newly segregated genera allowed the recognition of 322 different substances in 67 species of 10 genera. The chemical constituents most frequently found are sesquiterpene lactones, diterpenes and flavonoids, and the published biological activities of extracts and pure compounds were compiled. The detailed analysis, allowed us to identify that germacrolides, heliangolides, furanoheliangolides, and *ent*-kaurene-type diterpenes are the constituentus that best characterize this group of plants. Some comparisons between genera allowed to establish that furanoheliangolides are the type of sesquiterpene lactones that best characterize the genus *Aldama*. However, no direct relationships were identified between different genera and their chemical constituents.

The data obtained from the study of secondary metabolites will continue to be an essential source in collecting of comparative data for plant systematics. Some studies discussing phylogenetic relationships have shown congruence in the data obtained from the study of micro- (secondary metabolites) and macromolecules (DNA sequences) (*e.g*., Grayer et al. 1999). We recommend the analysis of a broader spectrum of species to reach more robust chemotaxonomic conclusions. The lack of substantial taxonomic information obtained among the secondary metabolites and species may be due to the low number of species studied to date. Therefore, complementary, large-scale phytochemistry (plant metabolomics) combined with bioinformatics undoubtedly will provide massive metabolite profiles that will have a major impact in many areas of scientific research, such, as systematics (Sumner *et al*. 2003).

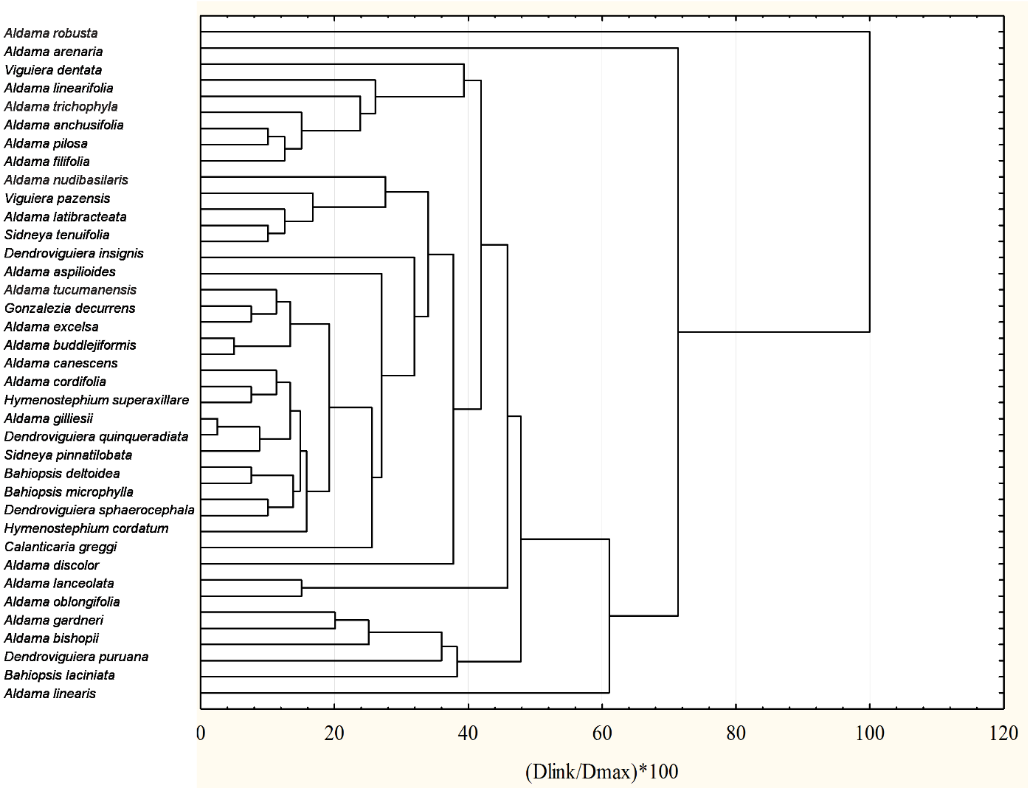


Figure 11. Classification of 38 species formerly classified in the genus *Viguiera* according to their content of four types of sesquiterpene lactones, and bi-, tri-, and tetra-terpenoids. The distance matrix was built with city-block (Manhattan) distances and the grouping algorithm was the unweighted pair-group average.

Supplementary material

Table S1. Species of *Viguiera s. l.* arranged according to the S. F. Blake's (1918) classification can be accessed here: https://doi.org/10.17129/botsci.3072

Acknowledgments

The authors acknowledge the support of the Universidad Nacional Autónoma de México (DGAPA PAPIIT IG200821), and we thank the students, co-workers and colleagues whose names are included in the references.

Literature cited

Álvarez L, Zamilpa A, Marquina S, González M. 2003. Two new oleanolic acid saponins from the roots of *Viguiera hypargyrea*. *Revista de la Sociedad Química de México* **47**: 173-177. ISSN: 1870-249X

Álvarez L, Mata R, Delgado G, Romo de Vivar A. 1985. Sesquiterpene lactones from *Viguiera hypargyrea*. *Phytochemistry* **24**: 2973-2976. DOI: https://doi.org/10.1016/0031-9422(85)80038-8

Ambrosio SR, Arakawa NS, Esperandin VR, de Albuquerque S, Da Costa FB. 2008. Trypanocidal activity of pimarane diterpenes from *Viguiera arenaria*. *Phytotherapy Research* **22**: 1413-1515. DOI: https://doi.org/10.1002/ptr.2512

Ambrosio SR, Tirapelli CR, Da Costa FB, de Oliveira AM. 2006. Kaurane and pimarane-type diterpenes from the *Viguiera* species inhibit vascular smooth muscle contractility. *Life Sciences* **79**: 925–933. DOI: https://doi.org/10.1016/j.lfs.2006.05.015

Ambrosio SR, Schorr K, Da Costa FB. 2004. Terpenoids of *Viguiera arenaria* (Asteraceae). *Biochemical Systematics and Ecology* **32**: 221-224. DOI: https://doi.org/10.1016/S0305-1978(03)00139-x

Ambrosio SR, Tirapelli CR, Bonaventura D, De Oliveira AM, Da Costa FB. 2002. Pimarane diterpene from *Viguiera arenaria* (Asteraceae) inhibit rat carotid contraction. *Fitoterapia* **73**: 484-489. DOI: https://doi.org/10.1016/S0367326X(02)001703

Arakawa NS, Schorr K, Ambrosio SR, Merfort I, Da Costa FB. 2008. Further sesquiterpene lactones from *Viguiera robusta* and the potential anti-inflammatory activity of a heliangolide: Inhibition of human neutrophil elastase release. *Zeitschrift für Naturforschung C* **63**: 533-538. DOI: https://doi.org/10.1515/znc20087811

Arellano-Martínez R, Delgado G. 2010. Hypargyrin A, a hemiacetalic germacrolide from *Viguiera hypargyrea* (Asteraceae). Biogenetic implication and biological evaluation. *Journal of the Mexican Chemical Society* **54**: 117-121.

Baldwin BG. 2009. Heliantheae alliance. *In*: Funk VA, Susanna A, Stuessy TF, Bayer RJ eds. *Systematics, Evolution and Biogeography of the Compositae*. Vienna, Austria: International Association for Plant Taxonomy (IAPT), pp. 689-711. ISBN: 978 3-9501754-3-1.

Blake SF. 1918. A revision of the genus *Viguiera*. *Contributions from the Gray Herbarium of Harvard University* **54**: 1-205. ~~DOI~~

Bohlmann F, Gerke T, Jakupovic J, King R, Robinson H. 1984a. Cadina-4,11-Diene from *Viguiera oblongifolia*. *Phytochemistry* **23**: 1183-1184. DOI: https://doi.org/10.1016/S0031-9422(00)82638-2

Bohlmann F, Zdero C, Schmeda G, Jakupovic J, Castro V, King R, Robinson H. 1984b. Heliangolide, Trachyloban- und Villanovan-Derivate aus Viguiera- Arten. *Liebigs Annalen der Chemie* 495-502.

Bohlmann F, Jakupovic J, Ahmed M, Grenz M, Suding H, Robinson H, King R. 1981. Germacranolides and Diterpenes from *Viguiera* Species. *Phytochemistry* **20**: 113-116. DOI: https://doi.org/10.1016/0031-9422(81)85228-4

Bohlmann F, Zdero C, Mahanta P. 1977. Neue diterpene aus *Dimorphoteca*- und *Viguiera*-arten. *Phytochemistry* **16**: 1073-1075. DOI: https://doi.org/10.1016/S0031-9422(00)86737-0

Bohm B, Stuessy TF. 2001. *Flavonoids of the Sunflower Family (Asteraceae)*. Wien: Springer. ISBN 3-211-834.

Bombo AB, Filartiga AL, Garcia VL, Appezzato-da-Gloria B. 2017. Secretory structures in *Aldama* species (Heliantheae-Asteraceae): morphology, histochemistry and composition of essential oils. *Flora* **228**: 39-49. DOI: https://doi.org/10.1016/j.flora.2017.01.011

Bombo AB, De Oliveira TS, De Oliveira ADSS, García RVL, Galvão MMA. 2012. Anatomy and essential oils from aerial organs in three species of *Aldama* (Asteraceae-Heliantheae) that have difficult delimitation. *Australian Journal of Botany* **60**: 632-642. DOI: http://dx.doi.org/10.1071/BT12160

Campos-Lozada V, Campos E, Guerrero C, Taboada J, Hernández-Falcon J, Fuentes-Pardo, B. 1993. Nonspecific anti-spasmodic action of viguiepinol. *Proceedings of the Western Pharmacology Society* **36**: 29-32.

Canales M, Hernández T, Rodríguez-Monrroy MA, Jiménez-Estrada M, Flores CM, Hernández LB, Gijón IC, Quiroz S, García AM, Avila G. 2008. Antimicrobial activity of the extracts and essential oil of *Viguiera dentata*. *Pharmaceutical Biology* **46**: 719-723. DOI: https://doi.org/10.1080/13880200802215727

Carvalho TC, Simão MR, Ambrosio SR, Furtado NAJC, Veneziani RCS, Heleno VCG, Da Costa FB, Gomes BPFA, Souza MGM, Dos Reis EB, Martins CHG. 2011. Antimicrobial activity of diterpenes from *Viguiera arenaria* against endodontic bacteria. *Molecules* **16**: 543-551. DOI: https://doi.org/10.3390/molecules160100543

Chagas-Paula DA, Oliveira TB, Vasconcelos Faleiro DP, Oliveira RB, Da Costa FB. 2015. Outstanding anti-inflammatory potential of selected Asteraceae species through the potent dual inhibition of cyclooxygenase-1 and 5-lipoxygenase. *Planta Medica* **81**: 1296-1307. DOI: https://doi.org/10.1055/s00351546206

Chen Y, Mulder PP, Schaap O, Memelink J, Klinkhamer PG, Vrieling K. 2022. The evolution of pyrrolizidine alkaloid diversity among and within Jacobaea species. *Journal of Systematics and Evolution* **60**: 361-376. DOI https://doi.org/10.1111/jse.12671

Cuevas LA, García Jiménez F, Romo de Vivar A. 1972. Structure of stenolobin. [A new diterpene from *Viguiera stenoloba*]. *Revista Latinoamericana de Química* **3**: 22-27.

Cuevas-Glory LA, Ortiz-Vazquez E, Pino JA, Sauri-Duch E. 2012. Floral classification of Yucatan Peninsula honeys by PCA & HS_SPME/GC-MS of volatile compounds. *International Journal of Food Science and Technology* **47**: 1378-1383. DOI: https://doi.org/10.1111/j.1365-2621.2012.02983.x

Cuevas-Glory LA, Pino JA, Sauri-Duch E. 2008. Volatile constituents of Tahoral flower (*Viguiera dentata* Blake, var. heliantioides) from Yucatan Peninsula, Mexico. *Journal of Essential Oil Research* **20**: 432-434. DOI: https://doi.org/10.1080/10412905.2008.9700050

Da Costa FB, Terfloth L, Gasteiger J. 2005. Sesquiterpene lactone-based classification of three Asteraceae tribes: A study based on self-organizing neutral networks applied to chemosystematics. *Phytochemistry* **66**: 345-353. DOI: https://doi.org/10.1016/j.phytochem.2004.12.006

Da Costa FB, Schorr K, Arakawa NS, Schilling EE, Spring O. 2001. Infraspecific variation in the glandular trichomes of two *Viguiera* species (Heliantheae; Asteraceae). *Journal of the Brazilian Chemical Society* **12**: 403-407. DOI: https://doi.org/10.1509/S0103-50532001000300012

Da Costa FB, Ito IY, Andre RFG, Vichnewski W. 1998. Constituents of *Viguiera* species with antibacterial activity. *Fitoterapia* **69**: 86-87.

Da Costa FB, Albuquerque S, Vichnewsky W. 1996a. Diterpenes and synthetic derivatives from *Viguiera aspillioides* with trypanomicidal activity. *Planta Medica* **6**: 557-559. DOI: https://doi.org/10.1055/s-2006-957971

Da Costa FB, Vichnewsky W, Herz W. 1996b. Constituents of *Viguiera aspillioides* and *Viguiera robusta*. *Biochemical Systematics and Ecology* **24**: 585-587. DOI: https://doi.org/10.1016/0305-1978(96)00057-9

De la Fuente JR, Del Valle MI, Sosa VE. 1994. Furanoheliangolides and flavonoids from *Viguiera mollis*. *Anales de la Asociación Química Argentina* **82**: 61-64.

Delgado G, Álvarez L, Mata R, Pereda-Miranda R, Romo de Vivar A, Villaseñor JL. 1986. Terpenoids from *Viguiera latibracteata* and *Viguiera greggii*. *Journal of Natural Products* **49**: 1165-1166. DOI: https://doi.org/10.1021/np50048a054

Delgado G, Álvarez L, Romo de Vivar A. 1985. 15-Hydroxy acetylerioflorin and other constituents from *Viguiera linearis*. *Phytochemistry* **24**: 2736-2738. DOI: https://doi.org/10.1016/S0031-9422(00)80712-8

Delgado G, Álvarez L, Romo de Vivar A. 1984a. 15-Oxo-zoapatlin, a diterpene lactone from *Viguiera maculata. Phytochemistry* **23**: 2674-2675. DOI: https://doi.org/10.1016/S0031-9422(00)84125-4

Delgado G, Álvarez L, Romo de Vivar A. 1984b. Terpenoids and flavan-3-ol from *Viguiera quinqueradiata*. *Phytochemistry* **23**: 675-678. DOI: https://doi.org/10.1016/S0031-9422(00)80405-7

Delgado G, Cárdenas H, Peláez G, Romo de Vivar A. 1984c. Terpenoids from *Viguiera excelsa* and *Viguiera oaxacana*. *Jounal of Natural Products* **47**: 1042-1045. DOI: https://doi.org/10.1021/np50036a028

Delgado G, Romo de Vivar A. 1984d. *Ent*-kaurenoid methyl esters from *Viguiera stenoloba* and its biometric conversion to zoapatlin. *Chemistry Letters* 1237-1240. DOI: https://doi.org/10.1246/cl.1984.1237

Delgado G, Romo de Vivar A, Cárdenas J, Pereda-Miranda R, Huerta E. 1984e. *Ent*-beyerene and *ent*-atisene diterpenes from *Viguiera insignis*. *Phytochemistry* **23**: 2285-22881. DOI: https://doi.org/10.1016/S0031-9422(00)80536-1

Delgado G, Romo de Vivar A, Ortega A, Cárdenas J, Schlemper EO. 1983. Diterpenoids from *Viguiera insignis*. *Phytochemistry* **22**:1227-1230. DOI: https://doi.org/10.1016/0031-9422(83)80227-1

Delgado G, Romo de Vivar A, Herz W. 1982. Sesquiterpene lactones from *Viguiera* species. *Phytochemistry* **21**: 1305-1308. DOI: https://doi.org/10.1016/0031-9422(82)80130-1

De Olveira ADS, Imamura PM, Ruiz ALTG, Appezzato-da- Gloria B, de Olveira TS, García VL. 2021. Antiproliferative activity from Aldama arenaria (Baker) EE Schill. & Panero. *Boletin Latinoamericano y del Caribe de Plantas Merdicinales y Aromáticas* **20**: 51-60. DOI: https://doi.org/10.37360/blacpma.21.20.1.4

De Oliveira TS, Bombo AB, De Oliveira ADSS, Garcia VL, Appezzato da Gloria B. 2016. Seasonal variation of the essential oil from two Brazilian native *Aldama* La Llave (Asteraceae) species. *Anais de Academia Brasileira de Ciencias* **88**: 1899-1907. DOI: https://doi.org/10.1590/0001-376520162015-0732

Dupuy OAL, Murillo R, Bonilla JA. 2008. Lactonas sesquiterpénicas de las plantas *Viguiera sylvatica* y *Decachaeta thieleana* (Asteraceae) modulan la producción de óxido nítrico y la fagocitosis de macrófagos RAW. *Revista de Biología Tropical* **56**: 1063-1073.

Domínguez XA, Ellmauerer E, Sánchez H, Franco OR, Verde SJ. 1988. *Viguiera superaxillare* (romerillo), a further source of cycloartanone derivative. *Revista Latinoamericana de Química* **19**: 144.

Emerenciano VP, Militao JSLT, Campos CC, Romoff P, Kaplan MAC, Zambon M, Brant AJC. 2001. Flavonoids as chemotaxonomic markers for Asteraceae. *Biochemical Systematics and Ecology* **29**: 947-957. DOI: https://doi.org/10.1016/S0305-1978(01)00033-3

Espinosa-García FJ, García-Rodríguez YM, Bravo-Monzón AE, Vega-Peña EV, Delgado-Lamas G. 2021. Implications of the foliar phytochemical diversity of the avocado crop *Persea americana* cv. Hass in its susceptibility to pests and pathogens. *PeerJ* 9:e11796 pp. 1-29. DOI: https://doi.org/10.7717/peerj.11796

Fattori V, Zarpelon AC, Staurengo-Ferrari, Borghi SM, Zaninelli TH, Da Costa FB, Alves-Filho JC, Cunha TM, Cunha FQ, Casagrande R, Arakawa NS, Verri Jr WA. 2018. Budlein A, a sesquiterpene lactone from *Viguiera robusta*, alleviates pain and inflammation in a model of acute gout arthritis in mice. *Frontiers in Pharmacology* **9**: 1076. DOI: https://doi.org/10.3389/fphar.2018.01076

Ferreira JH, García RM, Abrao F, Fernandez YA, Pires RH, Ambrosio SR, Veneziani RCS, Martins CHG. 2018. Bactericidal kinetics and antibiofilm efficacy of pimarane-type diterpenes from *Viguiera arenaria* against cariogenetic bacteria. *Pharmacognosy Journal* **10**: 429-434. DOI: https://doi.org/10.5530/pj.2018.3.70

Filartiga AL, Bombo AB, García, V. L., Appezzato da Gloria, B. 2017. Belowground organs of four Brazilian Aldama (Asteraceae) species: Morphoanatomical traits and essential oil profile. *South African Journal of Botany* **113**: 150-159. DOI: https://doi.org/10.1016/j.sajb.2017.08.008

Filartiga AL, Bombo AB, García VL, Appezzato da Gloria B. 2017b. Leaf and stem anatomy and essential oil composition of four Brazilian *Aldama* species (Asteraceae) and their taxonomic significance. *Brazilian Journal of Botany* **40**: 503-516. DOI: https://doi.org/10.1007/s40415-016-0350-3

Gao F, Wang H, Mabry TJ, Abboud KA, Simonsen SH. 1989. Sesquiterpene lactones, flavanones and a diterpene acid from *Viguiera laciniata*. *Phytochemistry* **28**: 2409-2414. DOI: https://doi.org/10.1016/S0031-9422(00)97994-9

Gao F, Wang H, Mabry TJ. 1987. Diterpenoids and a sesquiterpene lactone from *Viguiera ladibractate. Phytochemistry* **26**: 779-781. DOI: https://doi.org/10.1016/S0031-9422(00)84785-8

Gao F, Mabry TJ. 1986a. Sesquiterpene lactones from *Viguiera deltoidea*. *Phytochemistry* **25**: 137-140. DOI: https://doi.org/10.1016/S0031-9422(00)94518-7

Gao F, Mabry TJ, Bohlmann F, Jakupovic J. 1986b. Cycloartanone derivatives from *Viguiera dentata. Phytochemistry* **25**: 1489-1491. DOI: https://doi.org/10.1016/S0031-9422(00)81319-9

Gao F, Mabry TJ. 1985a. An acyclic diterpene from *Viguiera deltoidea*. *Phytochemistry* **24**: 3061-3063. DOI: https://doi.org/10.1016/0031-9422(85)80060-1

Gao F, Miski M, Gage DA, Mabry TJ. 1985b. Terpenoid constituents of *Viguiera dentata*. *Journal of Natural Products* **48**: 316-318. DOI: https://doi.org/10.1021/np50038a021

Gao F, Miski M, Gage DA, Norris JA, Mabry TJ. 1985c. Terpenoids from *Viguiera potosina*. *Journal of Natural Products* **48**: 489-490. DOI: https://doi.org/10.1021/np50039a026

García-Rodríguez YM, Bravo-Monzón A, Martínez-Díaz Y, Torres-Gurrola G, Espinosa-García F J. 2012. Variación Fitoquímica Defensiva en Ecosistemas Terrestres. In JC Rojas, EA Malo (Eds.), *Temas Selectos en Ecología Química de Insectos* (pp. 217–252). El Colegio de la Frontera Sur, México. ISBN: 13:9786077637714.

Gershenzon J, Dudareva N. 2007. The function of terpene natural products in the natural world. *Nature Chemical Biology* **3**: 408-414. DOI: https://doi.org/10.1038/nchembio.2007.5

Gershenzon J, Liu YL, Mabry TJ, Korp JD, Bernal I. 1984. Germacranolides from *Viguiera microphylla*. *Phytochemistry* **23**: 1281-1287. DOI: https://doi.org/10.1016/S0031-9422(00)97994-9

González MLM, Joray MB, Laiolo J, Crespo MI, Palacios SM, Ruiz GM, Carpinella MC. 2018. Cytotoxic activity of extracts from plants of Central Argentina on sensitive and multidrug-resistant Leukemia cells: Isolation of an active principle from *Gaillardia megapotamica*. *Evidence-Based Complementary and Alternative Medicine.* Article ID 9185935. DOI: https://doi.org/10.1155/20189185935

Grayer RJ, Chase MW, Simmonds MSJ. 1999. A comparison between chemical and molecular characters for the determination of phylogenetic relationships among plant families: an appreciation of Hegnauer's "Chemotaxonomie der Pflanzen." *Biochemical Systematics and Ecology,* **27**: 369-393. DOI: https://doi.org/10.1016/S0031-9422(00)97994-9

Guerreiro E. 1986. Heliangolides and acyclic diterpene from *Viguiera gilliesii*. *Phytochemistry* **25**: 748-750. DOI: https://doi.org/10.1016/0031-9422(86)88040-2

Guerrero C, Nava AL, Quevedo F, Toscano RA, Soriano-García M. 1986. Further constituents of *Viguiera stenoloba* and *Viguiera pinnalobata*. *Revista Latinoamericana de Química* **16**: 126-128.

Guerrero C, Santana M, Romo J. 1976. Chemical study of *Viguiera angustifolia* H. B. K. Blake. *Revista Latinoamericana de Química* **7**: 41-42.

Guerrero C, Ortega A, Díaz E, Romo de Vivar A. 1973. Structure of viguestenin and deacetylviguestenin. *Revista Latinoamericana de Química* **4**: 118-126.

Guillet G, Chauret D, Arnason JT. 1997. Phototoxic polyacetylenes from *Viguiera annua* and adaptations of a chrysomelid beetle, *Zygogramma continua*, feeding on this plant. *Phytochemistry* **45**: 695-699. DOI: https://doi.org/10.1016/S0031-9422(97)00030-7

Harborne JB, Smith DM. 1978. Anthochlors and other flavonoids as honey guides in the *Compositae*. *Biochemical Systematics and Ecology* **6**: 287-291. DOI: https://doi.org/10.1016/0305-1978(78)90047-9

Herz W, Kulanthaivel P. 1985. Diterpenes from *Viguiera porteri*. *Journal of Natural Products* **48**: 676-677. DOI: https://doi.org/10.1021/np50040a039

Heywood VH, Harborne JB, Turner BL eds. 1977. *The Biology and Chemistry of the Compositae*. Academic Press. New York. 2 vols. ISBN: 0123468019(v.1)

Hind DJN, Beentje HJ. eds. 1996. *Compositae: Systematics. Proceedings of the International Compositae Conference, Kew*, 1994. The Royal Botanic Gardens, Kew. 2 vols. ISBN: 13: 9781900347006.

Hu Y, Bajorath J. 2013. Compound promiscuity: what can we learn from current data? *Drug Disxovery Today* **18**: 645-650. DOI: http://dx.doi.org/10.1016/j.drudis.2013.03.002

Kato FH, Viana NI, Santini CB, Gomes de Souza CG, Veneziani RES, Ambrosio SR, Tavares DC. 2012. Assessment of the *in vitro* and *in vivo*genotoxic and antigenotoxic effect of pimaradienoic acid in mammalian cells. *Mutation Research-Genetic Toxicology and Environmental Mutagenesis* **749**: 87-92. DOI: https://doi.org/10.1016/j.mrgentox.2012.09.001

Langenheim JH. 1994. Higher plant terpenoids: a phytocentric overview of their ecological roles. *Journal of Chemical Ecology* **20**: 1223-1280. DOI: https://doi.org/10.1007/BF02059809

Liu YL, Gershenzon J, Mabry TJ. 1984. Furanoheliangolides from *Viguiera greggii*. *Phytochemistry* **23**: 1967-1970. DOI: https://doi.org/10.1016/S0031-9422(00)84951-1

Lüttmann-Skibinski H, Willuhn O. 1988. Diterpenes and other constituents of *Viguiera buddleiaeformis*. *Planta Medica* **54**: 578. DOI: https://doi.org/10.1055/s-2006-962590

Maffei M, Gertsch J, Appendino G. Plant volatiles: Production, function and pharmacology. 2011. *Natural Products Reports* **28**: 1359-1380. DOI: https://doi.org/10.1039/c1np00021g

Marangoni S, Moraes TS, Utera SH, Casemiro LA, De Souza MGM, De Oliveira PF, Veneziani P S, Ambrosio SR, Tavares DC, Martins CHG. 2018. Diterpenes of the pimarane type isolated from *Viguiera arenaria*: Promising *in vitro* biological potential as therapeutic agents for endodontics. *Journal of Pharmacognosy and Phytotherapy* **10**: 34-44. DOI: https://doi.org/10.5897/jpp2017.0475

Marquina M, Maldonado N, Garduño-Ramírez ML, Aranda E, Villareal ML, Navarro V, Bye R, Delgado G, Álvarez L. 2001. Bioactive oleanolic acid saponins and other constituents from the roots of *Viguiera decurrens*. *Phytochemistry* **56**: 93-97. DOI: https://doi.org/10.1016/S0031-9422(00)00283-1

Meragelman KM, Espinar LA, Sosa VE, Uriburu ML, De la Fuente JR. 1996. Terpenoid constituents of *Viguiera tucumanensis*. *Phytochemistry* **41**: 499-502. DOI: https://doi.org/10.1016/S0031-9422(95)00584-6

Mizokami SS, Hohmann MSN, Staurengo-Ferrari L, Carvalho TT, Zarpelon AC, Possebon MI, de Sousa AR, Veneziani RCS, Arakawa NS, Casagrande R., Verri WA. 2016. Pimaradienoic acid inhibits carrageenan-induced inflammatory leukocyte recruitment and edema in mice: Inhibition of oxidative stress, nitric oxide and cytokine production. *Plos One* **11**: e0149656. DOI: https://doi.org/10.1371/journal.pone.0149656

Nicolete R, Arakawa NS, Rius C, Nomizo A, Jose PJ, Da Costa FB, Sanz MJ, Faccioli LH. 2009. Budlein A from *Viguiera robusta* inhibits leukocyte-endothelial cell interactions, adhesion molecule expression and inflammatory mediators release. *Phytomedicine* **16**: 904-915. DOI: https://doi.org/10.1016/j.phymed.2009.04.002

Nogueira MS, Da Costa FB, Brun R, Kaiser M, Schmidt TJ. 2016. *Ent*-pimarane and *ent*-kaurane diterpenes from *Aldama discolor* (Asteraceae) and their antiprotozoal activity. *Molecules* **21**: 1237. DOI: https://doi.org/10.3390/molecules21091237

Ortega A, Lara R, Martínez R, Díaz E. 1980. Sphaerocephalin, a germacranolide isolated from *Viguiera sphaerocephala*. *Phytochemistry* **19**: 1545-1546. DOI: https://doi.org/10.1016/0031-9422(80)80217-2

Porto TS, Furtado NAJC, Heleno VCG, Martins CHG, Da Costa FB, Severiano ME, Silva AN, Veneziani RCS, Ambrósio SR. 2009a. Antimicrobial ent-pimarane diterpenes from *Viguiera arenaria* against Gram-positive bacteria. *Fitoterapia* **80**: 432-436. DOI: https://doi.org/10.1016//j.fitote.2009.06.003

Porto TS, Rangel R, Furtado NAJC, Carvalho TC, Martins CHG, Veneziani RCS, Da Costa FB, Vinholis AHC, Cunha WR, Heleno VCG, Ambrosio SR. 2009b. Pimarane-type diterpenes: Antimicrobial activity against oral pathogens. *Molecules* **14**: 191-199. DOI: https://doi.org/10.3390/molecules14010191

Possebon MI, Mizokami SS, Carvalho TT, Zarpelon AC, Hohmann MSN, Staurengo-Ferrari L, Ferraz CR, Hayashida TH, de Souza AR, Ambrosio SR, Arakawa NS, Casagrande R, Verri WA Jr. 2014. Pimaradienoic acid inhibits inflammatory pain: Inhibition of NF-κB activation and cytokine production and activation of the NO−Cyclic GMP−Protein kinase G−ATP-Sensitive potassium channel signaling pathway. *Jounal of Natural Products* **77**: 2488-2496. DOI: https://doi.org/10.1021/np500563b

Rieseberg LH, Schilling EE. 1985. Floral flavonoids and ultraviolet patterns in *Viguiera* (Compositae). *American Journal of Botany* **72**: 999-1004. DOI: https://doi.org/10.2307/2443442

Rocha ACFS, Morais GO, da Silva AA, Kovatch PY, Ferreira DS, Esperandim VR, Pagotti MC, Magalhães LG, Heleno VCG. 2022. *Natural Product Research* **36**: 875-884. Doi: https://doi.org/10.1080/14786419.2020.1837824

Romo de Vivar A., Pérez-Castorena AL, Arciniegas A, Villaseñor JL. 2007. Secondary metabolites from Mexican species of the Tribe Senecioneae (Asteraceae). *Journal of the Mexican Chemistry Society* **51**: 160-172.

Romo de Vivar A, Delgado G. 1985. Los metabolitos secundarios de *Viguiera* (Compositae, Heliantheae) química e implicaciones quimiotaxonómicas. *Boletín de la Sociedad Chilena de Química* **30**: 79-100.

Romo de Vivar A, Bratoeff E, Ontiveros E, Lankin DC, Bhacca NS. 1980. Viguilenin, a germacranolide from *Viguiera linearis*. *Phytochemistry* **19**: 1795-1797. DOI: https://doi.org/10.1016/S0031-9422(00)83815-7

Romo de Vivar A, Delgado G, Guerrero C, Reséndiz J, Ortega A. 1978. Study of Viguieras. Structure of viguiepinin and correction of viguiestenin. *Revista Latinoamericana de Química* **9**: 171-174.

Romo de Vivar A, Guerrero C, Díaz E, Bratoeff EA, Jiménez L. 1976. The germacranolides of *Viguiera buddleiaeformis.* Structures of budlein-A and -B. *Phytochemistry* **15**: 525-527. DOI: https://doi.org/10.1016/S0031-9422(00)88963-3

Schilling EE, Panero JL. 2011. A revised classification of subtribe Helianthinae (Asteraceae: Heliantheae) II. Derived lineages. *Botanical Journal of the Linnean Society*, **167**: 311-331. DOI: https://doi.org/10.1111/j.1095-8339.2011.01172.x

Schilling EE, Panero JL. 2002. A revised classification of subtribe Helianthinae (Asteraceae: Heliantheae) I. Basal lineages. *Botanical Journal of the Linnean Society*, **140**: 65-76. DOI: https://doi.org/10.1046/j.1095-8339.2002.00079.x

Schilling EE. 1989. External flavonoid aglycones of *Viguiera* series *Viguiera* (Asteraceae Heliantheae). *Biochemical Systematics and Ecology* **17**: 535-538. DOI: https://doi.org/10.1016/0305-1978(89)90096-3

Schilling EE, Panero JL. 1988a. Flavonoids of *Viguiera* Series *Brevifoliae*. *Biochemical Systematics and Ecology* **16**: 417-418. DOI: https://doi.org/10.1016/0305-1978(88)90036-1.

Schilling EE, Panero JL, Bhom BA. 1988b. Flavonoids of *Viguiera* Section *Maculatae. Biochemical Systematics and Ecology* **16**: 413-416. DOI: https://doi.org/10.1016/0305-1978(88)90035-X

Schmeda-Hirschmann G, Zdero C, Baruah RN, Bohlmann. F. 1985. Further sesquiterpene lactones from *Calea* and *Viguiera* species. *Phytochemistry* **24**: 2019-2022. DOI: https://doi.org/10.1016/S0031-9422(00)83114-3

Schorr K, García-Piñeres AJ, Siedle B, Merfort I, Da Costa, FB. 2002. Guaianolides from *Viguiera gardneri* inhibit the transcription factor NF-κB. *Phytochemistry* **60**: 733-740. DOI: https://doi.org/10.1016/S0031-9422(02)00128-0

Seaman F, Bohlmann F, Zdero C Mabry TJ. 1990. *Diterpenes of Flowering Plants: Compositae (Asteraceae)*. New York: Springer. ISBN-13: 978-1461279457

Seaman F. 1982. Sesquiterpene lactones as taxonomic characters in the Asteraceae. *Botanical Review* **48**: 121-595. DOI: https://doi.org/10.1007/BF02919190

Seigler D, Price PW. 1976. Secondary compounds in plants: primary functions. *American Naturalist* **110**: 101-105. DOI: https://doi.org/10.1086/283050

Selener MG, Elso O, Grosso C, Borgo J, Clavin M, Malchiodi EL, Cazorla SI, Redko F, Sülsen VP. 2019. Anti-trypanosoma cruzi activity of extracts from Argentinean Asteraceae species. *Iranian Journal of Pharmaceutical Research* **18**: 1854-1861. DOI: http://dx.doi.org/10.22037/ijpr.2019.14491.12430

Shimokoriyama M, Geissman TA. 1960. Anthochlor pigments. XIV. The pigments of *Viguiera multiflora* (Nutt.) and *Baeria chrysostoma* (F. and M.). *Journal of Organic Chemistry* **25**: 1956-1959. DOI: https://doi.org/10.1021/jo01081a0033

Shulha O, Zidorn Ch. 2019. Sesquiterpene lactones and their precursors as chemosystematic markers in the tribe Cichorieae of the Asteraceae revisited: an update. *Phytochemistry* **163**: 149-177. https://doi.org/10.1016/j.phytochem.2019.02.001

Soares ACF, Matos PM, Da Silva KF, Gomes Martins CHG, Sola Veneziani RC, Ambrosio SR, Dias, HJ, Dos Santos RA, Gomes Heleno VC. 2019a. Antimicrobial potential of natural and semi-synthetic ent-kaurane and ent-pimarane diterpenes against clinically isolated gram-positive multidrug-resistant bacteria. *Journal of Brazilian Chemical Society* **30**: 333-341. DOI: https://doi.org/10.21577/0103-5053.20180182

Soares ACF, Matos MP, Dias HJ, De Paula Aguiar G, Dos Santos ES, Gomes Martins CH, Sola Veneziani RC, Ambrosio SR, Gomes Heleno VC, 2019b. Variability of the antibacterial potential among analogue diterpenes against Gram-positive bacteria: considerations on the structure–activity relationship. *Canadian Journal of Chemistry* **97**: 568-575. DOI: http://dx.doi.org/10.1139/cjc-2018-0369

Spring O, Zipper R, Conrad J, Vogler B, Klaiber I, Da Costa FB. 2003. Sesquiterpene lactones from glandular trichomes of *Viguiera radula* (Heliantheae; Asteraceae). *Phytochemistry* **62**: 1185-1189. DOI: https://doi.org/10.1016/S0031-9422(02)00747-1

Spring O, Zipper R, Reeb S, Vogler B, Da Costa FB. 2001. Sesquiterpene lactones and a myoinositol from glandular trichomes of *Viguiera quinqueremis*. *Phytochemistry* **57**: 267-272. DOI: https://doi.org/10.1016/S0031-9422(01)00019-X

Spring O, Zipper R, Klaver I, Reeb S, Vogler B. 2000. Sesquiterpene lactones from *Viguiera eriophora* and *Viguiera puruana* (Heliantheae, Asteraceae). *Phytochemistry* **55**: 255-261. DOI: https://doi.org/10.1016/S0031-9422(00)00276-4

Spring O, Buschmann H. 1996. A chemotaxonomic survey of sesquiterpene lactones in the Helianthinae (Compositae). *In*: Hind DJN, Beentje HJ, eds. *Compositae: Systematics. Proceedings of the International Compositae Conference, Kew, Vol. 1. 1994.* United Kingdom: The Royal Botanic Gardens, Kew. pp. 307-316.

Sumner LW, Mendes P, Dixon RA. 2003. Plant metabolomics: large-scale phytochemistry in the functional genomics era. *Phytochemistry* **62**: 817-836. DOI: https://doi.org/10.1016/S0031-9422(02)00708-1

Tamayo-Castillo G, Jakupovic J, Bohlmann F, King RM. Boldt PE. 1990. Germacranolides and diterpenes from *Viguiera* species. *Revista Latinoamericana de Química* **21**: 67-69.

Tamayo-Castillo G, Jakupovic J, Bohlmann F, Castro V. 1989. Heliangolides from *Viguiera sylvatica*. *Phytochemistry* **28**: 2737-2740. DOI: https://doi.org/10.1016/S0031-9422(00)98079-8

Taylor PG, Dupuy Loo OA, Bonilla JA, Murillo R. 2008. Anticancer activities of two sesquiterpene lactones, millerenolide and thieleanin isolated from *Viguiera sylvatica* and *Decachaeta thieleana*. *Fitoterapia* **79**: 428-432. DOI: https://doi.org/10.1159/000074240

Tirapelli CR, Ambrosio SR, Da Costa FB, De Oliveira AM. 2004. Evidence for the mechanisms underlying the effects of pimaradienoic acid isolated from the roots of *Viguiera arenaria* on rat aorta. *Pharmacology* **70**: 31-38. DOI: https://doi.org/10.1159/000074240

Tirapelli CR, Ambrosio SR, Da Costa FB., De Oliveira AM. 2002. Inhibitory action of kaurenoic acid from *Viguiera robusta* (Asteraceae) on phenylephrine-induced rat carotid contraction. *Fitoterapia* **73**: 56-62. DOI: https://doi.org/10.1016/S0367-326X(01)00365-3

Torres-Gurrola G, García-Rodríguez YM, Lara-Chávez MBN, Guillen-Andrade H, Delgado G, Espinosa-García FJ. 2016. Análisis de la riqueza de metabolitos secundarios de *Persea* spp., bajo algunas hipótesis que proponen explicar la función de la diversidad fitoquímica, Capítulo 5, pp. 195-292. In: Anaya AL, Espinosa-García FJ, Reigosa Roger MJ (Coord.). *Ecología Química y Alelopatía: Avances y Perspectivas*. Instituto de Ecología, Universidad Nacional Autónoma de México -Plaza y Valdés, México, D.F. ISBN: 978-607-402-912-3.

Turner BL. 2015. Recension of *Viguiera* (sensu stricto) (Asteracese: Heliantheae) of Mexico. *Phytologia* **97**: 16-24.

Uriburu ML, Gil RR, Sosa VE, De la Fuente JR. 2008. Caffeoyl esters of threonic acid and its lactone from *Viguiera pazensis*. *The Journal of Argentinian Chemical Society* **96**: 55-61.

Vaccarini CE, Palacios SM, Meragelman KM, Sosa VE. 2002. Antifeedant activity of metabolites from *Viguiera tucumanensis*. *Natural Products Letters* **16**: 323-327. DOI: https://doi.org/10.1080/10575630290030711

Vaccarini CE, Palacios SM, Meragelman KM, Sosa VE. 1999. Phytogrowth-inhibitory activities of a clerodane from *Viguiera tucumanensis*. *Phytochemistry* **50**: 227-230. DOI: https://doi.org/10.1016/S0031-9422(98)00518-4

Valério DAR, Cunha TM, Arakawa NS, Lemos HP, Da Costa FB, Parada CA, Ferreira SH, Cunha FQ, Verri WA. 2007. Anti-inflammatory and analgesic effects of the sesquiterpene lactone budlein A in mice: Inhibition of cytokine production-dependent mechanism. *European Journal of Pharmacology* **562**: 155-163. DOI: https://doi.org/10.1016/j.ejphar.2007.01.029

Vasconcelos Faleiro DP, Casoti R, Chagas-Paula DA, Padilla-González GF, Barbosa de Olveira R, Da Costa FB. 2021. Metabolomic studies of *Aldama* spp and other Asteraceae species to identify dual inhibitors of cyclooxygenase-1 and 5-lipoxygenase. *Phytochemistry letters* **44**: 210-215. DOI: https://doi.org/10.1016j.phytol.2021.06.028

Villaseñor JL. 2016. Checklist of the native vascular plants of Mexico. *Revista Mexicana de Biodiversidad* **87**: 559-902. DOI: http://dx.doi.org/10.1016/j.rmb.2016.06.017

Wollenweber E, Dörr M, Roitman JN, Schilling E. 1995. External flavonoids of three species of *Viguiera* section *Hypargyrea* (Asteraceae). *Zeitschrift fuer Naturforschung C* **50**: 588-590. DOI: https://doi.org/10.1515/znc-1995-7-819

Zamilpa A, Tortoriello J, Navarro V, Delgado G, Álvarez L. 2002. Antispasmodic and antimicrobial diterpenic acids from *Viguiera hypargyrea* roots. *Planta medica* **68**: 281-283. DOI: https://doi.org/10.1055/s-2002-23146

Zarpelon AC, Fattori V, Souto FO, Pinto LG, Pinho-Ribeiro FA, Ruiz-Miyazawa KW, Turato WM, Cunha TM, da Costa FB, Cunha FQ, Casagrande R, Arakawa NS, Verri Jr WA. 2017. The sesquiterpene lactone, budlein A, inhibits antigen-induced arthritis in mice: Role of NF-κB and Cytokines. *Inflammation* **40**: 2020-2032. DOI: https://doi.org/10.1007/s10753-017-0642-1

Zdero C, Bohlmann F. 1990. Systematics and Evolution within the Compositeae, seen from the eyes of a chemist. *Plant Systematics Evolution* **171**: 1-14. DOI: https://doi.org/10.1007/BF00940593

Zidorn Ch. 2008. Sesquiterpene lactones and their precursors as chemosystematic markers in the tribe Cichorieae of the Asteraceae. *Phytochemistry* **69**: 2270-2296. DOI: https://doi.org/10.1016/j.phytochem.2008.06.013.

Associate editor: Arturo de Nova Vázquez

Author contributions:

AA, research design, data collection, writing of original draft; ALPC, review and editing; ARV, research design, review; LGG, data collection; FJEG, conceptualization, data analysis, review; JLV, conceptualization, data analysis, writing, review; GD, coordination, data analysis, writing, review. All authors have made substantial intellectual contributions for the data analyses and have approved the final version to be published.

Appendix 1. Secondary metabolites isolated from species of genus *Aldama*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Aldama anchusifolia (DC.) E.E. Schill. & Panero (=*Viguiera anchusifolia* (DC.) Baker)		**121, 138**	**206-208, 212, 215, 216, 221, 228, 229, 241**	SAM: Arg, Bol	Filartiga *et al*. 2017a, 2017b
Aldama angustifolia (Hook. & Arn.) Schill. & Panero (=*Viguiera angustifolia* (Hook. & Arn.) S.F. Blake)	**52**			MEX	Guerrero *et al*. 1976
Aldama arenaria (Baker) Schill. & Panero (=*Viguiera arenaria* Baker)	**52**	**125-132, 137**	**206-208, 211, 215, 216, 224, 229-231, 237, 239, 241, 243**	SAM: Braz	Ambrosio *et al*. 2004, Carvalho *et al*. 2011, De Oliveira *et al*. 2016
Aldama aspillioides (Baker) Schill. & Panero (=*Viguiera aspillioides* Baker)		**151, 159, 161-163, 166, 171, 173, 187**	**229**	SAM: Braz	Da Costa *et al*. 1996a, b
Aldama bishopii (H. Rob.) E.E. Schill. & Panero (=*Viguiera bishopii* H. Rob.)		**120-122, 139, 146, 151, 171, 177, 187, 191**	**206, 229, 233, 243, 300, 301**	SAM: Bol	Bohlmann *et al.* 1981
Aldama bracteata (Gardner) E.E. Schill. & Panero (=*Aldama quinqueremis* (S.F. Blake) E.E. Schill. & Panero; =*Viguiera quinqueremis* S.F. Blake)	**5, 6, 48-50, 52, 55, 69, 70, 74, 77-79, 87, 88**		**322**	SAM: Braz	Spring *et al*. 2001
Aldama buddlejiformis (DC) E.E. Schill. & Panero (=*Viguiera buddlejiformis* (DC.) Hemsl.)	**3, 52**	**148, 171, 173, 175**	**250, 286, 295**	MEX	Romo de Vivar *et al*. 1976, Lüttman-Skibinski & Willuhn 1988
Aldama canescens (B.L. Rob.) E.E. Schill. & Panero (=*Viguiera potosina* S.F. Blake	**111**	**148, 150, 169 170**		MEX	Gao *et al*. 1985c
Aldama cordifolia (A. Gray) E.E. Schill. & Panero (=*Viguiera cordifolia* A. Gray)		**139, 151**	**206, 207**	SW USA to MEX	Bohlmann *et al.* 1977
Aldama discolor (Baker) E.E. Schill. & Panero (=*Viguiera discolor* Baker)	**52**	**134-136, 183**	**206-208, 212, 214, 216, 218, 229, 232, 238, 242**	SAM: Braz	Nogueira *et al*. 2016, Bombo *et al.* 2017
Aldama excelsa (Willd.) E.E. Schill. & Panero (=*Viguiera excelsa* (Willd.) Benth. & Hook. f.)	**52**	**151, 172, 177-179, 184**	**234, 313**	MEX	Delgado *et al*. 1984c

Accepted name	**SLs**	**Diterpenes**	**Others**	**Distribution**	**References**
Aldama filifolia (Sch.Bip. ex Baker) E.E. Schill. & Panero (=*Viguiera filifolia* Sch. Bip. ex Baker)			**206, 208, 211, 229, 243**	SAM: Braz, Para	Bombo *et al*. 2012
Aldama gardneri (Baker) E.E. Schill. & Panero (=*Viguiera gardneri* Baker)	**16**, **101-105**		**259, 285, 310**	SAM: Braz	Schorr *et al*. 2002
Aldama gilliesii (Hook & Arn.) E.E. Schill. & Panero (=*Viguiera gilliesii* (Hook. & Arn.) Hieron.	**20, 21, 70**, **72, 73**	**113**		SAM: Arg	Guerreiro 1986
Aldama ghiesbreghtii (Hemsl) E.E. Schill. & Panero (=*Viguiera hemsleyana* S.F. Blake)	**55**			MEX	Delgado *et al*. 1982
Aldama helianthoides (Rich.) E.E. Schill. & Panero (=*Viguiera procumbens* (Pers.) S.F. Blake)	**3, 35, 36, 38, 51, 55, 69, 70**, **93**	**114, 115, 125, 151, 177, 187**	**227, 238, 242, 243, 246-248, 252, 308, 309**	SAM: Peru to Arg	Bohlmann *et al*. 1981, Schmeda-Hirschmann *et al.* 1985, Tamayo-Castillo *et al*. 1990
Aldama hypochlora (S.F. Blake) E.E. Schill. & Panero (=*Viguiera hypochlora* (S.F. Blake) S.F. Blake	**52**			MEX	Delgado *et al*. 1982
Aldama incana (Pers.) E.E. Schill. & Panero (=*Viguiera incana* (Pers.) S.F. Blake		**151**	**246, 247**	SAM. Ecu to Bol	Bohlmann *et al.* 1981
Aldama lanceolata (Britton) E.E. Schill. & Panero (=*Viguiera lanceolata* Britton)	**55**	**151, 187**	**246- 248**	SAM: Peru to Bol	Bohlmann *et al*. 1981, 1984a
Aldama latibracteata (Hemsl.) E.E. Schill. & Panero (=*Viguiera latibracteata* (Hemsl.) S.F. Blake	**64, 91**	**148, 149, 151, 152, 166, 169, 172, 174, 175 178, 181, 184**	**234, 313, 314**	MEX	Delgado *et al*. 1986, Gao *et al*. 1987
Aldama linearifolia (Chodat.) E.E. Schill. & Panero (=*Viguiera linearifolia* Chodat)		**151**	**206-208, 211-215, 217, 218, 222, 228, 229, 231, 241, 243**	SAM: Braz to Para	Tamayo-Castillo *et al*. 1990, Bombo *et al*. 2012
Aldama linearis (Cav.) E.E. Schill. & Panero (=*Viguiera linearis* (Cav.) Sch. Bip. ex Hemsl.)	**1, 3, 24, 26, 37, 38, 52**, **54**, **56**, **57**, **65**, **68**, **94**, **111**	**151, 168, 177, 178**	**229, 234**	MEX	Romo de Vivar *et al*. 1980, Delgado *et al*. 1985, Schmeda-Hirschmann *et al*. 1985

Accepted name	SLs	Diterpenes	Others	Distribution	References
Aldama mollis (Griseb.) E.E. Schill. & Panero (=*Viguiera molli*s Griseb.)	**58**, **76**		**251, 252**	SAM: Bol to NW Arg	De la Fuente *et al*. 1994
Aldama nervosa (Gardner) E.E. Schill. & Panero (=*Viguiera nervosa* Gardner)		**139, 150, 151**	**246**	SAM: Braz	Tamayo-Castillo *et al*. 1990
Aldama nudibasilaris (S.F. Blake) E.E. Schill & Panero (=*Viguiera nudibasilaris* S.F. Blake)		**138, 165**	**206, 211, 216, 218, 221, 229**	SAM: Braz	Filartiga *et al.* 2017a, 2017b
Aldama oblongifolia (Gardner) E.E. Schill. & Panero (=*Viguiera oblongifolia* Gardner)	**57**, **59**		**223, 225, 235, 246**	SAM: Braz	Bohlmann *et al*. 1984a, Tamayo-Castillo *et al*. 1990
Aldama pilosa (Baker) E.E. Schill. & Panero (=*Viguiera pilosa* Baker)		**121**	**206-208, 215. 216, 229, 243**	SAM: Braz	Filartiga *et al*. 2017a, 2017b
Aldama robusta (Gardner) E.E. Schill. & Panero (=*Aldama radula* (Baker) E.E. Schill & Panero; =*Viguiera radula* Baker; =*Viguiera robusta* Gardner)	**3, 10-14, 24, 26, 40, 41, 51,52, 54, 56, 57, 62, 64, 77, 95, 110**	**118, 121, 128, 148, 151, 159, 161, 162, 166, 175, 177,**	**206-209, 211, 214, 215, 218, 219, 227, 229, 232, 241, 242, 306, 307, 310, 312**	SAM: Braz	Da Costa *et al*. 1996a, 2001, Arakawa *et al.* 2008, Tirapelli e*t al*. 2002, De Nicolete *et al*. 2009, De Oliveira *et al*. 2016, Spring *et al*. 2003
Aldama squarrosa (Sch. Bip.) E.E. Schill. & Panero (=*Viguiera schultzii* S.F. Blake)	**52**			MEX	Delgado *et al*. 1982
Aldama trichophylla (Dusén) Magenta (=*Viguiera trichophylla* Dusén)		**139, 149, 151**	**206-208, 211-215, 217, 219, 229, 243**	SAM: Braz	Tamayo-Castillo *et al*. 1990, Bombo *et al*. 2012
Aldama tucumanensis (Hook. & Arn.) E.E. Schill. & Panero (=*Viguiera tucumanensi*s (Hook. & Arn.) Griseb.	**1, 24, 35, 39, 69**, **70**, **77**, **100**, **107**	**123, 124, 151, 176, 179**	**236, 306**	SAM: Bol to Arg	Meragelman *et al*. 1996, Vaccarini *et al*. 1999, 2002

Appendix 2. Secondary metabolites isolated from species of genus *Bahiopsis*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Bahiopsis chenopodina (Greene) E.E. Schill. & Panero (=*Viguiera chenopodin*a Greene)			**259, 260, 271, 281-283**	MEX	Schilling 1989
Bahiopsis deltoidea (A. Gray) E.E. Schill. & Panero (=*Viguiera deltoide*a (A. Gray) A. Gray)	**15, 69**, **70**	**112**	**258-260, 271, 281-283**	MEX	Gao & Mabry, 1985a, 1986a, Schilling 1989
Bahiopsis laciniata (A. Gray) E.E. Schill. & Panero (=*Viguiera laciniat*a A. Gray)	**24**, **42-47**, **108**	**112**	**255-258, 263, 268-270, 287, 294**	MEX	Harborne *et al*. 1978, Gao *et al*. 1989, Schilling, 1989
Bahiopsis lanata Kellogg (=*Viguiera lanat*a (Kellogg) A. Gray)			**259, 260, 281, 283**	MEX	Schilling 1989
Bahiopsis microphylla (Vasey & Rose) E.E. Schill. & Panero (=*Viguiera microphyll*a Vasey & Rose)	**19, 80**, **86**		**258-260, 271, 282**	MEX	Gershenzon *et al*. 1984, Schilling 1989
Bahiopsis parishii (Greene) E.E. Schill. & Panero (=*Viguiera parishi*i Greene)			**282, 291**	SW USA to MEX	Schilling 1989
Bahiopsis reticulata (S. Watson) E.E. Schill. & Panero (=*Viguiera reticulata* S. Watson)			**258, 279, 284**	USA	Schilling 1989
Bahiopsis subincisa (Benth.) E.E. Schill. & Panero (=*Viguiera subincis*a Benth.)			**259, 260, 264**	MEX	Schilling 1989
Bahiopsis tomentosa (A. Gray) E.E. Schill. & Panero (=*Viguiera tomentos*a A. Gray)			**258, 271, 282**	MEX	Schilling 1989
Bahiopsis triangularis (M.E. Jones) E.E. Schill. & Panero (=*Viguiera triangular*is M.E. Jones)			**258-260, 271, 281-283, 291**	MEX	Schilling 1989

Appendix 3. Secondary metabolites isolated from species of genus *Calanticaria*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Calanticaria bicolor (Blake) E.E. Schill. & Panero (=*Viguiera bicolor* S.F. Blake)			**252, 267, 277, 278, 286, 287, 289, 290, 294, 295**	MEX	Schilling & Panero 1988a
Calanticaria brevifolia (Greemn.) E.E. Schill. & Panero (=*Viguiera brevifolia* Greenm.)			**267, 277, 278, 286, 287, 289, 290, 294, 295**	MEX	Schilling & Panero 1988a
Calanticaria greggii (A. Gray) E.E. Schill. & Panero (=*Viguiera greggii* (A. Gray) S.F. Blake)	**66**, **83, 89**	**151, 152**	**252, 253, 258-260, 265, 267, 272, 274, 282, 286, 287, 289, 294, 295**	MEX	Liu *et al*. 1984, Delgado *et al*. 1986, Schilling & Panero 1988a

Appendix 4. Secondary metabolites isolated from species of genus *Dendroviguiera*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Dendroviguiera adenophylla (S.F. Blake) E.E. Schill. & Panero (=*Viguiera adenophylla* S.F. Blake)			**258-260, 267, 273, 274, 286, 287, 290, 294, 295**	MEX	Schilling *et al*. 1988b
Dendroviguiera eriophora (Greenm.) E.E. Schill. & Panero (=*Viguiera eriophora* Greenm.; =*Viguiera maculata* (Brandegee) S.F. Blake)	**22-24, 52**, **54**, **60**, **61**, **67, 82**	**148, 151, 182**	**258-260, 267, 273-276, 286, 287, 290, 292, 294, 295**	MEX	Delgado *et al*, 1982, 1984a Schilling *et al*. 1988b, Spring *et al*. 2000
Dendroviguiera insignis (Miranda) E.E. Schill. & Panero (=*Viguiera insignis* Miranda)		**139-142, 144, 145, 151, 177, 185**	**258, 259, 267, 273-275, 286, 287, 290, 292, 294, 295**	MEX	Delgado *et al*. 1983, 1984e, Schilling *et al*. 1988b
Dendroviguiera neocronquistii (B.L. Turner) E.E. Schill. & Panero (=*Viguiera neocronquistii* B.L. Turner)			**286, 287, 294, 295**	MEX	Schilling *et al*. 1988b
Dendroviguiera oaxacana (Greenm.) E.E. Schill. & Panero (=*Viguiera oaxacana* S.F. Blake)		**151, 177**	**286, 287, 294, 295, 313**	MEX	Delgado *et al*. 1984c, Schilling *et al*. 1988b
Dendroviguiera pringlei (Fernald) E.E. Schill. & Panero (=*Viguiera trachyphylla* S.F. Blake)			**258-260, 267, 274, 286, 287, 290, 292, 294, 295**	MEX	Schilling *et al*., 1988b
Dendroviguiera puruana (Paray) E.E. Schill. & Panero (=*Viguiera puruana* Paray)	**18, 22**, **24**, **26-34**, **109**		**258, 259, 274**	MEX	Schilling *et al*. 1988b, Spring *et al*. 2000
Dendroviguiera quinqueradiata (Cav.) E.E. Schill. & Panero (=*Viguiera quinqueradiata* (Cav.) A. Gray ex S. Watson	**24, 26, 52**	**149, 152**	**258-260, 273, 286, 287, 293, 294, 313**	MEX	Delgado *et al*. 1984b, Schilling *et al*. 1988b
Dendroviguiera sphaerocephala (DC.) E.E. Schill. & Panero (=*Viguiera sphaerocephala* (DC.) Hemsl.	**8, 22**		**258-260, 267, 274-276, 286, 287, 290, 292, 294, 295**	MEX	Ortega *et al*. 1980, Schilling *et al*. 1988b
Dendroviguiera splendens (Panero & E.E. Schill.) E.E. Schill. & Panero (=*Viguiera splendens* Panero & E.E. Schill.)			**286-289, 294, 295**	MEX	Schilling *et al.* 1988b
Dendroviguiera sylvatica (Klatt.) E.E. Schill. & Panero (=*Viguiera sylvatica* Klatt)	**24, 52, 57**, **63**, **75**, **81**, **84**, **90**, **92**, **96-99**	**116, 117, 151**	**320, 321**	CAM: CRica to Panamá	Tamayo-Castillo *et al*. 1989, Taylor *et al*. 2008

Appendix 5. Secondary metabolites isolated from species of genus *Gonzalezia*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Gonzalezia decurrens (A. Gray) E.E. Schill. & Panero (=*Viguiera decurrens* (A. Gray) A. Gray)		**151, 152**	**193-198, 258, 262, 299, 315**	MEX	Wollenweber *et al.* 1995, Marquina *et al*. 2001
Gonzalezia hypargyrea (Greenm.) E.E. Schill. & Panero (=*Viguiera hypargyrea* Greenm.)	**1-4**, **7, 9, 17**	**139, 151, 158, 177, 184**	**193-195, 197-200, 234, 239, 258-260, 313, 314**	MEX	Álvarez *et al*. 2003, 1985, Wollenweber *et al*. 1995, Zamilpa *et al*. 2002, Arellano-Martínez & Delgado 2010
Gonzalezia rosei (Greenm.) E.E. Schill. & Panero (=*Viguiera rosei* Greenm.)			**252, 253, 259, 261, 286**	MEX	Wollenweber *et al*. 1995

Appendix 6. Secondary metabolites isolated from species of genus *Helianthus*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Helianthus porteri (A. Gray) Pruski (=*Viguiera porteri* S.F. Blake)		**148, 149, 151, 155, 157, 164, 175**	**313, 314, 316-318**	SE USA	Herz *et al.* 1985, Tamayo-Castillo *et al.* 1990

Apendix 7. Secondary metabolites isolated from species of genus *Heliomeris*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Heliomeris annua (M.E. Jones) Cockerell (=*Heliomeris longifolia* Cockerell *var. annua (M.E. Jones) W.F.* Yates; = *Viguiera annua* (M.E. Jones) S.F. Blake)			**244, 245**	SW USA to MEX	Guillet *et al*. 1977
Heliomeris multiflora Nutt. (=*Viguiera multiflora* (Nutt.) S.F. Blake)			**267, 286, 287, 294, 295, 302, 305**	USA to MEX	Shimokoriyama *et al*. 1960

Appendix 8. Secondary metabolites isolated from species of genus *Hymenostephium*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Hymenostephium cordatum (Hook. & Arn.) S.F. Blake (=*Viguiera cordata* (Hook. & Arn.) D'Arcy)	**52**, **68**, **85**, **91**	**151**	**227**	MEX to SAM: Colombia	Bohlmann *et al.* 1984b
Hymenostephium superaxillare S.F. Blake (=*Viguiera superaxillaris* (S.F. Blake) B.L. Turner		**139, 151, 177**	**205, 226**	MEX	Domínguez *et al*. 1988

Appendix 9. Secondary metabolites isolated from species of genus *Sidneya*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	SLs	Diterpenes	Others	Distribution	References
Sidneya pinnatilobata (Sch. Bip.) E.E. Schill. & Panero var. *megaphylla* (Butterw. ex B.L. Turner) E.E. Schill. & Panero (=*Viguiera pinnatilobata* (Sch. Bip.) S.F. Blake var. *megaphylla* Butterw. ex B.L. Turner)	**22, 23, 54**	**133**		MEX	Romo de Vivar *et al.* 1978, Guerrero *et al*. 1986
Sidneya tenuifolia (A. Gray) E.E. Schill. & Panero (=*Viguiera stenoloba* S.F. Blake)	**25**, **38**	**119, 139, 149, 151-153, 156, 176, 177, 180**	**239**	USA to CAM: El Salvador	Cuevas *et al*. 1972, Guerrero *et al*. 1973, 1986, Delgado & Romo de Vivar 1984d, Tamayo-Castillo *et al*. 1990
Sidneya tenuifolia (A. Gray) E.E. Schill. & Panero var. *chihuahuensis* B.L. Turner (=*Viguiera stenoloba* S.F. Blake var. *chihuahuensis* Butterw.)		**149-152, 192**	**244, 249**		Bohlmann *et al*. 1977

Appendix 10. Secondary metabolites isolated from species of genus *Viguiera*, arranged according to the new taxonomic circumscriptions and their geographical distribution. SAM= South America, MEX= Mexico, USA= United States of America. Numbers indicate the structure of the chemical constituent (see formulae below), considering the type of main constituents (SLs, diterpenes and others).

Accepted name	**SLs**	**Diterpenes**	**Others**	**Distribution**	**References**
Viguiera dentata (Cav.) Spreng. (=*Viguiera grammatoglossa* DC.)	**71**	**121, 139, 143, 144, 148, 151, 152, 167, 171,-177, 187**	**201-204, 206-209, 211, 214, 215, 217, 219, 220-222, 225, 227, 229, 237, 240, 241, 316**	SW USA to CA: Honduras	Bohlmann *et al*. 1977, 1981, Gao *et al*. 1985b, 1986b, Canales *et al.* 2008, Cuevas-Glory *et al*. 2008, 2012
Viguiera pazensis Rusby	**25, 53, 58**, **106**	**139, 144, 149, 152-154, 186, 190**	**246, 248, 254, 266, 296-299, 302-304, 311, 319**	SAM: Perú to Chile	Bohlmann *et al*. 1981, 1984b, Uriburo *et al*. 2008